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AN INVITATION FROM THE PRESIDENT.

It is a privilege and a pleasure to extend a cordial invitation to the members of the AMERICAN PHARMACEUTICAL ASSOCIATION, their families and friends, and to all others interested in the progress and well-being of Pharmacy, to attend the Eighty-Seventh Annual Meeting of the ASSOCIATION and the meetings of the Affiliated Organizations, in Atlanta, during the week of August 20, 1939.

As has been emphasized in previous years, these sessions cover every phase of Pharmacy. They provide a post-graduate course of instruction, and they make it possible for pharmacists from every section of our country to meet and interchange experiences. Prominent speakers will bring valuable messages, and the reports of officers and committees cover matters of vital concern to everyone engaged in the profession of Pharmacy.

The Program of the meeting is given in full in this issue of the JOURNAL and an examination of it will indicate how important this convention will be to every branch of the profession. Progress and problems are intermingled. Many of the latter need careful consideration and early attention. To reach sound decisions about these questions and to support them with a solid front is necessary to continued progress. It is hoped, therefore, that the attendance will be large and representative.

The pharmacists of Atlanta and of the State have arranged an excellent program of entertainment. The ASSOCIATION has not met in Georgia for many years, and in the meantime this section has made wonderful progress. In addition to the instructive business sessions, there are many places and things of interest to be seen and visited. Our generous hosts, renowned for their southern hospitality, have made provision for our convenience and comfort. Every one who can attend will find a cordial welcome.

J. LEON LASCOFF.

A MESSAGE FROM THE CHAIRMAN OF THE HOUSE OF DELEGATES.

This year, possibly more than ever before in the history of American Pharmacy, it is imperative that every pharmaceutical organization entitled to a seat in the House of Delegates of the AMERICAN PHARMACEUTICAL ASSOCIATION, should send delegates to represent its pharmacists at the greatest of all pharmaceutical forums. Atlanta will be the host city from the 20th to the 26th of August, and offers splendid entertainment and transportation facilities.

Economic, social and professional changes are no longer taking place from year to year, but rather from day to day, and if Pharmacy is to maintain its enviable position as one of the essential health sciences and continue to improve the pharmaceutical service to physicians and the public, its practitioners must get together and decide upon ways and means for doing promptly—*not* what *should* be done—but what *must* be done to preserve our autonomy. The questions most important to Pharmacy will be considered at this meeting—socialized medicine, food, drug and cosmetic legislation, modernization of pharmacy laws, public relations, U. S. P. and N. F. promotion—and many others.

American Pharmacy wants an expression of opinion from your pharmacists on these and many other vital questions and earnestly solicits your advice and suggestions on ways and means of consolidating and protecting its present position and of attaining greater strength with which to better discharge our professional responsibilities. It is only by universally-agreed-upon plans of action that our objectives can be reached.

CHARLES H. ROGERS.

A MESSAGE FROM THE LOCAL SECRETARY.

The entire South is looking forward to the meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION when it convenes in the Biltmore Hotel, Atlanta, Ga., during the week of August 20th–26th.

The last meeting of this body to be held in Georgia was in 1878 when the scars left by the Civil War were apparent on every hand. These scars were not confined to material things but were in evidence in the souls of men, all of which have disappeared and no section of America can boast of finer national spirit than is evidenced in the South.

The pharmacists of the South are looking forward with much anticipation to this meeting, most of whom have not had the opportunity to familiarize themselves with the splendid work of this parent ASSOCIATION, and the indications are that large numbers of pharmacists from every southern state will be present at some time during the course of the meeting.

The Biltmore Hotel will be general headquarters for all meetings and it is amply able to care for the comfort of all who will attend. Each room in the hotel is equipped with an overhead electric fan and air circulating systems are available in all meeting rooms. August is a hot month in any section of the United States, but the weather in Georgia at this season is more comfortable than is usually true in many other sections. Every bedroom in the Biltmore is an outside room and since the hotel is located a mile or more from the business center of Atlanta, the temperature is usually several degrees lower than that in the business center and usually, particularly at night, refreshing breezes are in evidence.

Plans for the entertainment and comfort of the visitors to Atlanta have been laid with a view in mind of making every feature distinctly southern in type so as to give some visual manifestation of true southern hospitality.

Plans are on foot to have in the lobby of the hotel a display of typical Georgia products the diversified nature of which will be of much educational value. It is planned to provide many souvenirs of these Georgia products for all who wish them.

The Governor of the State, the Chancellor of the University System of Georgia and others prominent in Georgia life will address the various groups, and efforts will be made to bring the visitors into close personal contact with the citizens of Atlanta and Georgia who are not necessarily identified with Pharmacy.

It is the hope of every Georgia pharmacist and of every Georgian that this meeting will prove to be the most pleasant and most profitable one in the history of the AMERICAN PHARMACEUTICAL ASSOCIATION, and to all who attend its meetings.

ROBERT C. WILSON.

FEDERAL FOOD, DRUG AND COSMETIC ACT REGULATIONS REVISED.

Changes in the general regulations promulgated under the Federal Food, Drug and Cosmetic Act and published in the Federal Register of December 28, 1938, have been approved by the Secretary of Agriculture. Regulation (c) under section 502(d) of the Act has been changed in accordance with an Act of June 23, 1939, which requires the declaration of the names, and quantities *or* proportions, instead of the names, quantities *and* percentages, of the habit-forming drugs enumerated in section 502(d) of the Act.

This new regulation was made necessary by the passage of an amendment to the Food, Drug and Cosmetic Act approved June 23, 1939, which changed the text of the statute so as to require a label declaration of the name, quantity *or* proportion of certain specified drugs, instead of the name, quantity *and* percentage. The same amendment postponed the new labeling provisions of the Food, Drug and Cosmetic Act until January 1, 1940, as well as the requirement that none but U. S. certified coal-tar colors may be used in foods, drugs and cosmetics. The amendment also authorized the Secretary of Agriculture to issue a regulation further postponing some of the requirements of the new statute until July 1, 1940, under certain conditions.

Regulation (c)(2) under section 502(e) of the Act has been revised by changing the temperature at which the percentage of alcohol is to be calculated from 68° Fahrenheit (20° Centigrade) to 60° Fahrenheit (15.56° Centigrade) so as to conform to the standard temperature for the determination of the percentage of alcohol recognized in the internal revenue law. Other minor editorial changes for the purpose of clarification, as well as the correction of some typographical errors, are also included.

These revisions will be published in the June 30th issue of the *Federal Register*, which can be obtained from the Superintendent of Documents, Government Printing Office, Washington, D. C. The price of a single copy is 10 cents.

THE ASSOCIATION FOR THE ADVANCEMENT OF PROFESSIONAL PHARMACY.

The June meeting was held at the Hotel Dauphin, on the 27th. The following were elected to office for the coming year: *President*, Dr. L. J. Piccoli; *First Vice-President*, Dr. F. D. Lascoff; *Second Vice-President*, Fred S. Frankfurter; *Third Vice-President*, Cyrus D. Hakes; *Treasurer*, Albert Klingmann; and *Secretary*, Irving Kantor.

The next regular meeting will be held at the Hotel Empire, September 19th. Following a resolution which was adopted by the members to give full coöperation during National Pharmacy Week, it was decided that in preparation for National Pharmacy Week the September meeting would be devoted to a program exclusively for building up the Prescription Department. Prominent speakers will be invited and there will be demonstrations on various types of shelf-stock bottles, standard references, simple manufacturing equipment, prescription typewriters, various types of labels, bottles and other accessories used in the compounding of prescriptions.

IRVING KANTOR, *Secretary*.

SECTIONS

BOARD OF REVIEW OF PAPERS (SCIENTIFIC SECTION).—*Chairman*, F. E. Bibbins; H. M. Burlage, W. G. Crockett, E. V. Lynn, C. O. Lee, L. W. Rising, L. W. Rowe, Heber W. Youngken, Ralph E. Terry, Carl J. Klemme.

A PHYTOCHEMICAL STUDY OF KALMIA ANGUSTIFOLIA L.*

BY M. L. JACOBS[1] AND W. R. LLOYD.[2]

Kalmia angustifolia L. is a small, hardy shrub growing in the Atlantic Coast States from Labrador to Ontario and southward through Pennsylvania, Virginia and the Carolinas to Alabama (1). It is known in various regions by the synonyms *Wichy, Sheep Laurel, Wicky, Lambkill, Dwarf Laurel* and *Sheepkill*. It contains a poisonous principle which is common to the species of Kalmia and which occurs in many Ericaceæ. This poison acts upon both man and animal, with the exception of the deer and the grouse. The flesh of the deer or grouse which has eaten the leaves is, however, poisonous to man. Holmes (2) reports the Cree Indians of the Hudson Bay area used *K. angustifolia* as a tonic, and the leaves have also been used as an arterial sedative and for the itch (3).

In 1886, Deibert (4) identified arbutin in the leaves of *K. angustifolia*. In the benzin extract, he reported *a wax, a resin* and *a fixed oil*. Stabler (5) and Bullock (6) and Matusow (7) reported studies of the constituents of *Kalmia latifolia* L., a similar shrub which grows somewhat larger than *K. angustifolia*. A survey of the literature reveals three characteristic compounds frequently present in members of the Ericaceæ. These are *arbutin, andromedotoxin* and *ursolic acid*. Kennedy (8) reported arbutin in *K. latifolia*, and Deibert (4) and Tunnman (9) reported arbutin in the leaves of *K. angustifolia*. Deibert (4) and Plugge (10) have reported andromedotoxin present in *K. angustifolia*.

The constituents present in the two species of Kalmia which have been reported in the literature are shown in Table I.

TABLE I.—CONSTITUENTS OF KALMIA AS REPORTED IN THE LITERATURE.

Constituent.	K. latifolia.	K. angustifolia.
Wax	Present (8)	Present (4)
Fixed oil	.....	Present (4)
Volatile oil	Present (5)	.....
	Absent (6)	.....
Andromedotoxin (phlorhizin)	Present (7, 10)	Present (4, 10)
Arbutin	Present (8)	Present (4, 9)
Tannin	Present (7, 11)	Present (4)
Phlobaphene	Present (7)	.....
Resin	Present (7)	Present (4)
Mucilage	Present (7)	Present (4)

Since *Kalmia angustifolia* grows widely in eastern North Carolina, and was therefore readily available, it was chosen for study in a series of North Carolina

* Presented before the Scientific Section, A. PH. A., Minneapolis meeting, 1938.

[1] From the Department of Pharmaceutical Chemistry, University of North Carolina, School of Pharmacy.

[2] Based upon a thesis submitted to the Graduate School of the University of North Carolina in partial fulfilment of the requirements for the degree of Master of Science.

plants having possible medicinal use. The leaves were gathered in Duplin County, near Rose Hill, North Carolina, and at three different times, August 1936, February 1937 and July 1937. The plants used in this study were identified by Dr. H. R. Totten of the Department of Botany of the University of North Carolina.

EXPERIMENTAL.

Ash Determinations.—The total ash and acid insoluble ash determinations were run by the U. S. P. XI methods and the results are shown in Table II. A qualitative analysis of the ash disclosed the presence of potassium, sodium, calcium, iron and magnesium as metals, and sulfates, chlorides and carbonates as acid radicals.

Moisture Determination.—The distillation with xylene method (12) was used to determine the moisture content of the plant. The results are shown in Table II. The ash determinations were then recalculated upon the basis of the moisture-free drug, and these results are shown in Table II.

TABLE II.—CONSTANTS OF KALMIA ANGUSTIFOLIA L.

I. Gathered August 1936 and February 1937.
II. Gathered July 1937.

Calculated on the Basis of Air-Dried Drug.

Total Ash.		Acid Insoluble Ash.	
I	2.80% av.	I	0.407% av.
II	2.99% av.	II	0.634% av.

Moisture.

I	7.30% av.
II	7.29% av.

Calculated on the Basis of Moisture-Free Drug.

Total Ash.		Acid Insoluble Ash.	
I	3.02% av.	I	0.439% av.
II	3.22% av.	II	0.683% av.

The Process of Stas-Otto.—Twenty grams of the air-dried drug were subjected to the process of Stas-Otto (13) by boiling with 100 cc. of alcohol made faintly acid with tartaric acid for half an hour under a reflux. After cooling and filtering, the alcoholic filtrate was evaporated to dryness, and the residue was taken up in water, and the aqueous solution extracted with ether. The aqueous solution was then treated with the following alkaloidal reagents and no precipitate was formed in any case: phosphotungstic acid, mercuric chloride, picric acid, iodine-potassium odide, Froehde's reagent, Mayer's reagent or tannic acid. A precipitate was formed with phosphomolybdic acid which is characteristic in the test for arbutin with ammonium hydroxide and phosphomolybdic acid. This failure to obtain positive tests was taken to indicate the absence of alkaloids.

The ether solution was then evaporated to dryness, and the residue was taken up in water. When treated with a few drops of 20% alpha-naphthol in alcoholic solution and sulfuric acid, a violet ring was produced at the junction of the solution and the acid, which indicates the presence of carbohydrates or glucosides.

The General Method.—Three portions of 400 Gm., 700 Gm. and 1200 Gm. of the air-dried drug were extracted separately in the continuous extraction apparatus of Wester (14) with petroleum ether, ether, chloroform and alcohol until extraction was complete. The amounts obtained in these extracts are shown in Table III. Each extract was then investigated according to the procedure outlined below.

TABLE III —EXTRACTS OF KALMIA ANGUSTIFOLIA OBTAINED BY CONTINUOUS EXTRACTION.

Petroleum ether	8.41% av.
Ether	2.59% av.
Chloroform	0.69% av.
Alcohol	28.75% av.

Petroleum Ether Extract.—The petroleum ether extract was saponified with alcoholic potassium hydroxide on a water-bath under a reflux. The saponification mixture was then poured into water and allowed to stand over night, and the mixture was extracted with ether. The ether layer (A) was then dried over anhydrous sodium sulfate.

The aqueous solution (B) was then acidified, and the precipitate filtered off. The filtrate was then extracted with ether and the ether layer was added to the above precipitate (C) and the whole evaporated to dryness. This residue was taken up in alcoholic potassium hydroxide and precipitated with lead acetate (15). The lead salts formed were extracted with ether, and the ether soluble lead salts (D) on evaporation proved to be in too small a quantity to be worked with. The ether insoluble lead salts (E) were suspended in water and decomposed with hydrochloric acid and extracted with ether. The ether solution so obtained yielded only crystals of potassium chloride.

The aqueous filtrate from the extraction of the saponifiable matter was allowed to evaporate to dryness, and the residue extracted with a mixture of three volumes of alcohol and one volume of ether. On evaporation, the residue was tested for glycerin with potassium acid sulfate, but the tests were negative.

The ether soluble, non-saponifiable fraction (A) was evaporated to dryness. Thirty-five grams of the petroleum ether extract yielded 25 Gm. of this residue. The residue was treated with hot alcohol, a residue (G) of 10 Gm. being insoluble. The hot alcohol solution (H) was then allowed to cool.

The insoluble portion (G) was treated with boiling acetic anhydride, two layers forming. The insoluble portion was separated from the solution while hot, and this portion cooled to a brown wax-like solid, melting at 48–50° C. From the melting point and the behavior toward solvents this substance was concluded to be a hydrocarbon (15). The acetic anhydride layer deposited a precipitate on cooling, and on the addition of water, precipitation was complete. On recrystallization from alcohol, it darkened and decomposed.

On cooling, the hot alcohol solution (H) formed 0.2 Gm. of a yellowish precipitate (K) which on recrystallization from alcohol and acetone gave a solid melting at 73° C. The acetate of this substance melted at 62° C. The substance did not give a positive Liebermann-Burchard test for sterols, so it was concluded to be an alcohol. Ceryl alcohol melts at 79° C. and its acetate melts at 65° C. While wet, this substance held a large volume of the solvent used to crystallize it from, but on drying, it decreased considerably in volume. This behavior is characteristic of carnaübyl alcohol, which melts at 68° C. (15).

The cold alcohol solution (L) was evaporated to dryness and the residue was taken up in benzene. On concentration, this solution yielded a white precipitate which on recrystallization from alcohol melted at 134° C., and gave a positive Liebermann-Burchard test for sterols. The acetate melted at 121° C. Sitosterol and its acetate melt at 136° C. and 125° C. respectively. The substance was concluded to be sitosterol (15).

On evaporation, the benzene solution yielded a brown, sticky mass, which when steam distilled gave no evidence of a volatile component.

Ether Extract.—A greenish white precipitate was noticed in the solvent reservoir during the extraction of the drug with ether. This precipitate was removed from the extract before concentration, and was recrystallized from alcohol as the potassium salt. On purification, this substance melted at 275° C. and gave a positive Liebermann-Salkowski test (16). This behavior on extraction, the melting point and the Liebermann-Salkowski test indicated ursolic acid. The substance was converted into the acetyl derivative which melted at 196° C., agreeing with that of the diacetyl derivative of ursolic acid (201° C.).

The ether was then removed from the remainder of the ether extract and the residue taken up in 10% potassium hydroxide solution. The mixture was filtered, and the aqueous solution (C) was precipitated with acid, and the mixture again filtered. This aqueous solution was precipitated with lead acetate, and since no further precipitate was given with lead subacetate, the mixture was filtered and the filtrate freed from lead with hydrogen sulfide. The aqueous solution was then extracted with chloroform. On evaporation of the solvent, a resinous substance resulted which could not be obtained in a crystalline form, but which gave a yellow color with sulfuric acid, turning red on heating; a blue color with hydrochloric acid; and a red

color with phosphoric acid. These color reactions are characteristic of andromedotoxin (phlorhizin).

The aqueous solution (D) was then evaporated to dryness under reduced pressure, and the residue was extracted with alcohol. On evaporation, a resinous substance was found which could not be obtained in a crystalline form, but which gave a blue color with ferric chloride and a blue color with ammonia and phosphomolybdic acid. These tests are characteristic of arbutin (10). Further attempts to obtain the glucosides in a crystalline form met with the same results.

Chloroform Extract.—The chloroform extract after the removal of the solvent was heated with water on a bath of water. The aqueous solution so obtained was evaporated to dryness, but again no crystalline substance could be obtained. The resinous substance so obtained gave the above tests for andromedotoxin.

Alcohol Extract.—Fifty grams of the alcohol extract after the removal of the solvent were taken up in 50 cc. of alcohol and precipitated with 100 cc. of ether. The precipitate (A) was removed and taken up in water. A residue (D) was left behind which was taken up in potassium hydroxide solution and precipitated with acid. 2.5 Gram. of phlobaphene were thus obtained. On heating in alcoholic solution with acid, the phlobaphene reduced Fehling's solution.

The aqueous solution (C) of the ether precipitate was then precipitated with lead acetate and lead subacetate and the lead precipitates were filtered off. These precipitates were then suspended in water, and decomposed with acid The mixture was then extracted with ethyl acetate, and the solvent removed. After several such treatments, an amorphous red tannin was obtained, which when dissolved in water, gave a greenish black color with ferric chloride and a flesh-colored precipitate with bromine water. These tests are characteristic of catechol tannins (17).

Treatment of the aqueous solution from the extraction of the tannins, and the ether soluble portion (B) of the alcohol extract by the method outlined above for the isolation of arbutin, yielded the same resinous substance as before, which gave the characteristic tests for arbutin.

Quantitative Determination of Tannins.—The total tannins present in the leaves of *K. angustifolia* were determined by the gravimetric method of Schröder (18), in which a water soluble percolate of the leaves is treated with hide powder for the complete absorption of the tannins. The leaves of *K. angustifolia* were found to contain 6.51% tannin.

Quantitative Determination of Glucosides.—One hundred fifty grams of the air-dried leaves were extracted with 200 cc. of boiling water and the decoction on cooling was precipitated with lead acetate and lead subacetate. The precipitates were filtered off and the solution freed from lead with hydrogen sulfide, and the aqueous solution so obtained evaporated to a volume of 50 cc. under reduced pressure. This solution was extracted with chloroform and 0.1 Gm. of phlorhizin obtained, amounting to 0.066% of the total weight of the air-dried drug.

The concentrated solution was then allowed to evaporate to dryness in the air, and the residue taken up in alcohol and boiled with charcoal. On evaporation, this solution yielded 1.4 Gm. of a resinous substance which gave positive tests for arbutin. This amounted to 0.93% of the total weight of the air-dried drug.

SUMMARY.

The total ash, acid insoluble ash, moisture and the inorganic constituents of the drug have been determined. A hydrocarbon, an alcohol and sitosterol were found in the petroleum ether extract. Ursolic acid and traces of andromedotoxin (phlorhizin) and arbutin were identified in the ether extract. Phlorhizin was identified in the chloroform extract. In the alcohol extract, catechol tannins, phlobaphene and arbutin were identified. The total tannins were determined to be 6.51%, the total content of andromedotoxin (phlorhizin) was found to be 0.066% and the total content of arbutin was found to be 0.93%.

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BIOASSAY OF PHENOLPHTHALEIN USING THE RHESUS MONKEY.*

BY K. A. BARTLETT[1] AND R. H. HERBINE.[1]

Being interested in laxatives in general, and especially phenolphthalein, we were very desirous of having some satisfactory method for evaluation of laxative action. A review of the literature showed that no satisfactory chemical assay was available and that all animals tried in connection with bioassays were not satisfactory, with one exception. The work of Fleig (1), back in 1908, suggested that it would be interesting to try experimental work on the monkey and twenty-six years later the work of Williams, Abramowitz and Killian (2) which, to our knowledge, is the first real work utilizing the monkey, showed definite promise of the development of a satisfactory bioassay. However, this work was not carried on to the point of establishing a definite assay method.

In view of the monkey showing more possibility than any other animal, we decided to further study the monkey in the hope that we might be able to develop a satisfactory bioassay method for laxatives. Our work over the past two years has enabled us to develop a satisfactory method for determining the relative potency of various samples of phenolphthalein. While this work has been conducted particularly in connection with phenolphthalein, we have found in our experiments that the rhesus monkey responds to Epsom Salts, Milk of Magnesia, Cascara, Castor Oil and Aloes. The method which has been evolved and which we are using at the present time follows.

We are using animals not commonly used in drug assays and believe it desirable to go into more detail concerning this method than would normally be considered necessary.

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* Presented at the Scientific Section, A. PH. A., Minneapolis meeting, 1938.

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Animals.—Our colony consists of twenty-three rhesus monkeys, thirteen males and ten females. Although we use the name "rhesus" which is commonly used in describing this type monkey, the specific name is Macaca mulatta (Zimmermann) (3).

Our animals are of various ages and weights, ranging from estimated ages of one and a half to five years old and from 1.5 to 5 Kg. in weight.

When new animals are purchased, they are isolated for a month and very closely observed. Almost half of the animals which we have purchased were rejected during this isolation period and we have had no deaths or signs of ill health in any of the animals which we have accepted and added to our regular colony. The presence of tuberculosis is the reason for the rejection of the majority of the animals during this isolation period. All the animals in our regular colony have gained considerable weight. Some of the older animals have more than doubled their weight. This, in itself, is an excellent criteria of their good health and contentment.

We have never purchased any monkeys which were entirely free from intestinal parasites. A few of the animals had only round worms. Most of them, however, had both round worms and hookworms. We originally thought that test animals used for this type work should be entirely free from all intestinal parasites and although we have spent considerable time in attempting to free these animals of these parasites, we have not been able to find an anthelmintic which is one hundred per cent effective against hookworms. However, we do have some animals which originally had only round worms and are now entirely free from these intestinal parasites, and we have observed that the results obtained on these worm-free animals are no more significant than those obtained upon the infested animals. There is, therefore, a question as to the importance of this point.

We have been unable to observe any difference in results obtained from either sex. If future experience bears out this observation, we feel that females will probably predominate because it has been our experience that females are more friendly, less nervous and easier to handle. We have been unable to observe any abnormal effects on administering phenolphthalein to females during the menstrual period. However, as our females become older this observation may be reversed.

Housing and Care.—The monkey laboratory is completely isolated from the rest of the plant. It is kept under lock and key at all times and only the immediate attendants are admitted. The animals are at no time teased, scolded or annoyed in any way.

The cages are 30″ square, 42″ in height and each is equipped with a swing, perch and removable front and sides. The bottoms are of expanded metal, the openings of which are large enough to allow the droppings to fall through into a removable metal tray.

A temperature of 75–85° F. is maintained whenever possible. Our cages are comparatively large and because of their size and their being equipped with a swing and perch, it is not necessary to have a so-called exercising cage.

The laboratory is so situated that it is entirely exposed on all four sides and although there is an abundance of light and fresh air, the animals are at no time exposed to direct sunlight. However, in our opinion, our diet adequately makes up for a lack of direct sunlight. On this question of direct sunlight, it is interesting to note that Mr. Otto Heinzer, caretaker of the Department of Pathology, Harvard Medical School has kept four rhesus monkeys in good health for a period of eight years in an indoor laboratory cage 5′ x 4′ x 3′. The diet used was very similar to the one we are using.

Diet.—The morning (9 A.M.) and evening (5 P.M.) meals each day consist of giving each animal approximately 4 fluidounces of milk-egg mixture (2 eggs per quart of milk prepared with Klim Powdered Whole Milk according to label directions). The noon meal is varied as follows:

Sat., Sun. & Mon.	Tues. & Wed.	Thurs. & Fri.
1 banana	1 banana	1 banana
1/4 head cabbage (med.)	1 small apple	1 small apple
1 small apple	spinach & carrot tops	1/2 head lettuce (med.)
	1/2 carrot	
	1/4 orange	

The food given at the noon meal is sprinkled with about one teaspoonful of bone meal and blood meal (equal parts). Every morning with the milk, each animal receives one White's Cod

Liver Oil Concentrate Tablet. The amounts of food are only tentative and we vary these amounts to suit the individual monkey. We try not to overfeed the animals but endeavor to give them just enough food to satisfy them and no more. Occasionally between feedings several grains of dried corn are given to the animals. With this diet the animals normally have stools of a putty-like consistency.

Technique.—We have tried several methods of administering the phenolphthalein doses to the animals. The one which we have found to be most satisfactory is to deposit the weighed amounts of phenolphthalein in the center of a small, $^3/_8$", cube of apple. In administering this cube of apple containing phenolphthalein, we find it only necessary to hold the apple cube in front of the cage. The animal will readily take and eat the entire cube. A cube of plain apple is given almost immediately after.

We have found that two doses can be administered to the animals each week. At the present time we administer doses on Mondays and Thursdays. All doses are administered immediately following the morning milk feeding. Stool examinations are made every hour after administration for six hours and also a twenty-four hour reading is made, noting the consistency of the stools.

Our results are either positive or negative, being based on passage of stools which are noticeably different (more fluid) then the normal stools which have a putty-like consistency. Sometimes these stools are very watery and without any form, and, on the other hand, they may be soft and though they do not have any definite form they do not run or spread as do the watery ones. Therefore, a negative reaction consists of the passage of no stools or of a stool of normal consistency within twenty-four hours, and a positive reaction consists of the passage of a soft stool or a watery, unformed movement within twenty-four hours.

Standardization of Animals.—The first goal of our work was to standardize all the test animals, that is determine the minimum (threshold) dose which will produce the desired effect. All dosages are based on the body weight of the animals—allowances are made of any gain in weight from week to week. In establishing this minimum effective dose, the animals were first given 1.0 mg. per Kg. of body weight of phenolphthalein, increasing the dosage gradually thereafter until the minimum effective dosage was reached (see Table I).

TABLE I.—DETERMINATION OF THRESHOLD DOSES OF INDIVIDUAL MONKEYS.

Animal Number.													Threshold Dose.
2	1.5	2.0	2.5	3.0	3.0	3.5	3.5	3.5	3.5	3.5	3.5	3.5	*3.5*
	N	N	N	W	N	N	W	W	S	S	W	W	
4	2.0	3.0	3.5	3.5	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0	*4.0*
	N	N	W	N	W	W	S	S	S	W	S	W	
7	1.0	2.0	3.0	4.0	5.0	6.0	6.5	7.0	7.0	7.0	7.0	7.0	*7.0*
	N	N	N	N	N	N	S	W	W	S	S	S	

All doses are in mg. per Kg. of body weight.
N = normal.
S = soft.
W = watery.

Each animal was standardized following the above procedure and Table II shows the standardization figures for the individual animals.

A sample of phenolphthalein has been set aside by us and we are arbitrarily recognizing this as standard reference phenolphthalein.

A number of assays were then conducted using our standardized monkeys and the standard phenolphthalein in the following manner. Nine standardized monkeys were divided into three groups of three animals each, one group was given their respective threshold doses, another group 75% of their respective threshold doses and the third group received 125% of their respective threshold doses. Stool observations were made in accordance with the procedure previously outlined. The results of each assay (potency index[1]) were calculated by adding the percentage

[1] Potency Index—Comparative laxative response obtained in an assay in terms of response produced by standard phenolphthalein (taken as 100).

TABLE II.—INDIVIDUAL THRESHOLD DOSES.

Animal No.	Sex.	Mg. per Kg. of Body Weight.
1	F	2.5
2	F	3.5
3	F	3.0
4	F	4.0
7	M	7.0
8	M	3.6
9	M	3.5
10	M	6.0
11	M	6.5
13	M	2.5
16	M	5.5
17	F	2.5
19	F	4.5
20	F	3.0
23	M	1.8

positive reaction of the three groups together and dividing by two. The following potency indices were obtained:

105.0, 75.0, 105.0, 105.0, 105.0, 120.0, 90.0, 120.0, 100.0, 100.0, 93.7, 83.3; average, 100.08.

By applying interpretative mathematics (4) to these results we obtain the following biometric expressions which indicate the accuracy of the method.

True Mean, 100.08; Average Deviation, 9.83; Probable Error, 8.31; Chance to be taken (5), 1 in 100.

Applying these expressions to the accepted formula

$$N = \left(\frac{K \times PE}{Diff.}\right)^2$$

we find that the degree of accuracy is 10.58%. This means that we are able to detect a variation of 10.58% or more in potency when using nine animals, and that the chance of error is 1 in 100.

PROPOSED METHOD OF ASSAY.

Animals.—The colony should contain at least twenty-one rhesus monkeys (macaca mulatta) of either sex and weighing between 1 and 5 Kg. Each animal should be housed in an individual cage and all animals should be fed exactly the same diet. Before conducting assays, all animals must be individually standardized with a standard reference sample of phenolphthalein. (Although only eighteen animals are used in conducting an individual assay, it is advisable to maintain at least three additional animals.) In the interests of accuracy, periodic re-standardization of animals is suggested.

Procedure.—Immediately following the morning meal, give reference phenolphthalein to nine animals and the unknown to an additional lot of nine animals. Three animals from each group are given their threshold dose (standardization dose), three are given 75% of their threshold dose and three are given 125% of their threshold dose. The doses are given in a small $^3/_8$" cube of apple.

Examine the individual cages at hourly intervals for six hours, and at twenty-four hours, noting the consistency of stools. A negative reaction consists of the passage of no stool or of a stool of normal consistency within twenty-four hours. A positive reaction consists of the passage of a soft stool or of a watery unformed movement within twenty-four hours.

Interpretation.—Add the percentage of positive reactions obtained in the three groups of animals receiving reference phenolphthalein and divide by two to obtain the potency index. If this value is not 100 make proper adjustments in interpretation. Similarly add the percentage of positive responses with the unknown at the three dosage levels and divide by two to obtain the

potency index of the unknown. Divide the potency index of the reference standard phenolphthalein by that of the unknown to determine their relative potency.

Results not falling within the range of error previously determined for the reference standard can only be considered indicative of the unknown potency. Adjustments of the unknown dosage level are then necessary and the assay re-run at this adjusted level.

DISCUSSION.

Subsequent reports will be presented covering the assays of unknown samples of phenolphthalein and other laxative substances.

We believe that the rhesus monkey is as near the ideal test animal for laxatives as is possible to find. This is borne out by the fact that the mg. per Kg. doses required by the monkey when calculated on the basis of the human are practically identical.

CONCLUSIONS.

1. A procedure for the bioassay of phenolphthalein using the rhesus monkey has been developed and found satisfactory.
2. Individual rhesus monkeys require different threshold doses of phenolphthalein.
3. This bioassay method might be found applicable to all other laxatives.

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PHARMACEUTICAL USES OF THE GLYCOLS AND THEIR DERIVATIVES.*

BY A. G. DUMEZ.[1]

The use of the glycols and their derivatives in Pharmacy is of comparatively recent origin but is increasing rapidly or was, until the occurrence of the "Elixir of Sulfanilamide" tragedies, a little more than a year ago. While it is a fact that ethylene glycol was prepared by Wurtz (1) in 1859 and that its possibilities as a substitute for glycerol were called attention to by a number of investigators over the next fifty or sixty years, little, if any, consideration was given to it or to the glycols prepared later (2) until after the World War. Prior to this time, alcohol was the solvent generally used by pharmaceutical manufacturers. It was cheap, there were no burdensome restrictions on its use and it was deemed to be as satis-

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factory as could be expected in other ways. With the passage of the Federal laws governing the manufacture, sale and use of alcohol which followed our entry into the War, these conditions changed. A heavy tax was placed upon alcohol and the restrictions thrown about its use were made more exacting, the first of which increased the initial cost and the second of which increased the cost of handling. The increase in production costs to the manufacturer as a result of these changes coupled with a decrease in price of the glycols as a result of the development of more economical methods of manufacture and of production on a large scale paved the way for the more general use in Pharmacy of the glycols and their derivatives.

In view of the fact that the glycols and their derivatives possess certain advantages over alcohol, *i. e.*, most of them are excellent general solvents possessing to a degree the combined solvent properties of both, alcohol and water, boil over a fairly wide range of temperatures, et cetera, it is astonishing that an economic stimulus was required to drive manufacturers to their use. It may be assumed, however, that the apparent inertia on the part of the pharmaceutical manufacturers in particular was not due so much to their unwillingness to avail themselves of the advantages offered by these new solvents as to fear of the injury which might be done to the products manufactured or to the users thereof through the use of untried materials. That this fear was well founded is borne out by the fatalities which resulted from the use of the elixir heretofore mentioned and by the more recent work done on the pharmacology and toxicology of these compounds (3),

Just when the glycols and their derivatives were first used in Pharmacy, I have not been able to discover, but it can be stated that their use in pharmaceutical manufacturing was antedated by their use as solvents in the lacquer industry for which some of the glycols and their alkyl ethers were being produced on a commercial scale twelve or more years ago (4). Further, that the first use of glycols in articles intended for human consumption was as a vehicle in flavoring essences and that this also occurred twelve or more years ago (5). Ten years ago, Lawrie (6) wrote ethylene glycol is now being produced synthetically in large quantities but there is not a wide market for it and, in 1932, Seidenfeld and Hanzlik (7) reported that, although propylene glycol is obtainable commercially, it has commanded little or no interest in Chemistry and Medicine. From the foregoing, it seems safe to assume that the use of the glycols and their derivatives in Pharmacy does not go back farther than ten years. That there has been a marked increase in the extent of their use in this field in the last five years is indicated by the increasing frequency with which they are mentioned in the literature covering this period.

The glycols which have been suggested as suitable for use in Pharmacy and those which are actually being used at the present are the lower members of the series, those containing less than six carbon atoms, and the derivatives used or suggested for use are certain ethers, alkyl esters and amino derivatives of these lower members. Taken together, they make quite a formidable list as is shown in the following table. The higher members of the series have evidently not received attention because most of them are solids at ordinary temperatures and the boiling points are beyond the desirable range.

The properties of the compounds listed which make them especially suitable for pharmaceutical use may be summarized briefly as follows: Most of them are

TABLE I.—GLYCOLS AND DERIVATIVES USED OR SUGGESTED FOR USE.

W = water. s. s. = slightly soluble.
A = alcohol. v. s. = very soluble.
E = ether. ins. = insoluble.
∞ = soluble in all proportions.

Name of Compound.	Chemical Formula.	Physical State. (ord. temp.)	Boiling Point. (approx.)	Solubility.
Ethylene glycol	$HOCH_2.CH_2OH$	Col. liq	197.2° C.	∞ W, ∞ A, 7.89 E
Ethylene glycol monoacetate	$CH_3COOCH_2.CH_2OH$	Col. liq.	182° C.	∞ W, ∞ A, E
Ethylene glycol monomethyl ether	$CH_3OCH_2.CH_2OH$	Col. liq.	124 °C.	∞ W, v. s. A, s. E
Ethylene glycol monoethyl ether	$C_2H_5OCH_2.CH_2OH$	Col. liq.	135.1° C.	∞ W, ∞ A, ∞E
Ethylene glycol monoethyl ether acetate	$CH_3COOCH_2.CH_2OC_2H_5$	Col. liq.	156.2° C.	22W, ∞ A, ∞ E
Ethylene glycol diethyl ether	$C_2H_5OCH_2.CH_2OC_2H_5$	Col. liq.	123° C.	
Ethylene glycol monobutyl ether	$C_4H_9OCH_2.CH_2OH$	Col. liq.	170.6° C.	∞ W, ∞ A, ∞ E
Ethylene glycol monophenyl ether	$C_6H_5OCH_2.CH_2OH$	Liquid	165° C.	
Diethylene glycol	$HOCH_2CH_2.O.CH_2CH_2OH$	Col. liq.	244.5° C.	s. W., s. A., s. E
Diethylene glycol dilaurate	$(C_{11}H_{23}COOC_2H_4)_2O$	Yel. liq.	250° C.	Disp. W, ∞ A, ∞ E
Diethylene glycol dioleate	$(C_{17}H_{33}COOC_2H_4)_2O$	Oily liq.	.....	Disp. W, ∞ A, ∞ E
Diethylene glycol distearate	$(C_{17}H_{35}COOC_2H_4)_2O$	White solid	.....	Disp. W, ins. A., ins. E
Diethylene glycol monoethyl ether	$CH_3OCH_2CH_2OCH_2.CH_2OH$	Col. liq.	193.2° C.	∞ W, v. s. A, s. E
Diethylene glycol monobutyl ether	$C_4H_9OCH_2CH_2OCH_2.CH_2OH$	Col. liq.	231.2° C.	∞ W, v. s. A, v. s. E
Trimethylene glycol	$HOCH_2CH_2CH_2OH$	Visc. liq.	214° C.	∞ W, ∞A, v. s. E
Trimethylene glycol methylene ether	$OCH_2OCH_2CH_2CH_2$	Col. liq.	105 °C.	∞ W, ∞ A, ∞ E
Triethylene glycol	$(CH_2OCH_2CH_2OH)_2$	Col. liq.	280°–290° C.	∞ W, ∞ A, s.s. E
Triethylene glycol monoethyl ether	$C_2H_5OCH_2CH_2OCH_2.CH_2OH$	Col. liq.	197° C.	∞ W, ∞ A
Ethanolamine	$HOCH_2.CH_2NH_2$	Col. liq.	172.2° C.	∞ W, ∞ A, 0.72 E
Triethanolamine	$N(CH_2CH_2OH)_3$	Visc. liq.	277° C.	∞ W, ∞ A, s. s. E
Propylene glycol	$CH_2OH.CHOHCH_3$	Col. liq.	189° C.	∞W, ∞ A, s. E
α-Butylene glycol	$CH_3CH_2CH(OH).CH_2OH$	Liquid	192 °C.	s. s. W, ∞ A
Pseudobutylene glycol	$CH_3CH(OH)CH(OH)CH_3$	Liquid	184° C.	∞ W, ∞A, ∞ E
Isobutylene glycol	$(CH_3)_2C(OH)CH_2OH$	Liquid	177° C.	s. W
β-Amylene glycol	$CH_3CH_2CH(OH)CH(OH)CH_3$	Liquid	187° C.	s. W., s. A
α-Isoamylene glycol	$(CH_3)_2CHCH(OH)CH_2OH$	Liquid	206° C.	s. A., s. E
β-Isoamylene glycol	$(CH_3)_2C(OH)CH(OH)CH_3$	Thick liq.	177° C.	∞ W, ∞A, ∞E

liquid at ordinary temperature; they are almost odorless or the odor is not objectionable; the taste is not objectionable, being sweetish as a rule; they boil at temperatures ranging from about 105° C. to 290° C.; most of them possess to a degree the combined solvent properties of alcohol and water; they can be dehydrated by heating; they inhibit the growth of microörganisms (8) when diluted and may, therefore, be used as preservatives; some of them, the esters of the higher fatty acids and the ethanolamines, are good emulsifying agents.

The above enumerated properties suggest as possible pharmaceutical uses for these compounds their utilization as solvents for the preparation of simple solutions and as menstrua for the extraction of drugs, as vehicles for carrying medicaments in solution or in suspension, as emulsifying agents for the preparation of creams and ointment bases and as preservatives for medicinal preparations. That these possibilities are steadily developing into actualities is revealed by the following information obtained from the available literature or from other sources.

Etylene Glycol.—As early as 1917, Bachem (9) stated that ethylene glycol was worthy of consideration as a substitute for alcohol in preparations containing iodine whether intended for

external or internal use. He also reported that it "mixes" readily with phenol, mercuric chloride, tannin, potassium iodide, tincture of iodine, lactic acid, salicylic acid, boric acid, menthol, thiogenol, tumenol, ichthyol and soap but not with fats and ethereal oils. Further, that it has been used successfully in mixture with ointments, with gelatin suppository bases and in the preparation of enemas, surgical dressings, cosmetics and preparations intended for local application in the nose, vagina and anal fissures.

In 1924, Fuller (10) called the attention of American manufacturers to the possibilities of using ethylene glycol as a substitute for alcohol in the manufacture of liquid medicinal preparations and reported that it possessed bacteriostatic properties.

In 1931, Hanzlik and co-workers (11), as a result of investigations on ethylene glycol as a substitute for glycerol, reached the conclusion that the former is an excellent general solvent; dissolves salts readily, many heavy metal salts, barbital, alkaloids, iodine, etc., and that it makes collodion pliable.

John Rae (12), in 1933, reported the results of experiments on the extraction of vegetable coloring matters with ethylene glycol. The results showed the glycol to be superior to alcohol in the extraction of the coloring matter of cudbear, red saunders, red rose petals, madder, saffron, Brazil wood, henna and cochineal.

In the February 13, 1932, number of the *Journal of the American Medical Association*, there appeared the advertisement of a well-known pharmaceutical manufacturer for a preparation to be used in the treatment of syphilis. This advertisement carried the statement that the preparation was a solution of sodium iodobismuthite in ethylene glycol (13). It is reported that propylene glycol is now used in place of ethylene glycol. A solution of sodium bismuthate in propylene glycol has been suggested as a more satisfactory preparation by Hanzlik and coworkers (14).

In 1936, Dr. Hinton (15) reported successful results in the treatment of inflammatory processes with a paste composed of magnesium sulfate and ethylene glycol.

A manufacturer of glycols (16) has supplied the information that anhydrous ethylene glycol is used to prepare sterile solutions of the barbiturates and that it is a suitable solvent for benzocaine in conjunction with acetylsalicylic acid.

Ethylene Glycol Monoethyl Ether.—As far back as 1927 (17), attention was called to the possible use of monoethyl ether of ethylene glycol as menstruum for the preparation of galenicals and for the extraction of the pungent principles of drugs and spices. Numerous references to its use in the preparation of cosmetics will be found in "Cosmetic Dermatology" by Goodman.

Ethylene Glycol Monoacetate.—This glycol ester has been suggested for use in the separation of medicinal paraffin from the other paraffines and is stated to be a good solvent for the essential oils (18), but there is no evidence that it is now being used for either of these purposes.

Diethylene Glycol.—Although frequently referred to in the literature as a good solvent for medicinals, there is no evidence to show that it is in actual use for this purpose at the present time.

Diethylene Glycol Monoethyl Ether.—This compound has been suggested as a suitable solvent for benzocaine in conjunction with acetylsalicylic acid (19). Stable solutions which do not require alcohol are said to be thus obtained.

Diethylene Glycol Dilaurate, Dioleate and Distearate.—Diethylene glycol oleate is used for making solutions of oils and for the preparation of emulsions of both, the oil in water and water in oil types (20).

The dilaurate is used as a solvent for oil-soluble dyes where the latter are to be incorporated in an aqueous mixture, to replace sulfonated oils in pharmaceuticals and cosmetics and for the preparation of emulsions. A special grade (neutral) with a p_H of 6.9 is prepared for the pharmaceutical and cosmetic trades (20).

The distearate is reported to be an excellent emulsifying agent for fatty oils, hydrocarbons and waxes. It disperses in hot water with the production of viscous fluids or creams, hence it may be used to replace the vegetable gums, tragacanth, karaya and quince, in certain types of preparations. It is used in the cosmetic industry for the preparation of lotions and creams. In pharmaceutical manufacturing, it is also used as a lubricant or to provide a protective coating for hydroscopic powders, crystals, tablets, troches, etc. It is used in nebulæ and ointment bases to make possible the removal of greasy stains by washing with water (20).

Triethanolamine.—Within the last five or six years, triethanolamine, which may be looked upon as an amino derivative of three molecules of ethylene glycol, has developed from a laboratory curiosity into a commercial product of many and varied applications. In certain respects, it exhibits the combined properties of glycerol and ammonia. It is used for the preparation of cosmetic emulsions (21) and in dermatologic therapy (22). In Pharmacy, it is used in the form of the stearate for the preparation of ointment bases. A formula for a paraffin oil emulsion intended for internal use in which triethanolamine stearate is the emulsifying agent selected has been elaborated by Norstroem (23).

Trimethylene Glycol Methylene Ether.—Jordan (24) states that this glycol ether is used for the extraction of ethereal oils and is a good solvent for many substances used in Pharmacy.

Triethylene Glycol.—While this glycol has been suggested as a solvent which might have some pharmaceutical application, there is no evidence of its use at the present time (25).

Propylene Glycol.—It was suggested by Hanzlik and co-workers (26) in 1931 that propylene glycol offered possibilities as a solvent or vehicle for medicinal preparations.

In 1935, Brown (27) summarized the conclusions which he reached after a fairly comprehensive study of the suitability of this glycol as a solvent for pharmaceutical use as follows:

1. "In assaying propylene glycol galenicals, involving the use of ether or chloroform for extraction, the galenical should be diluted with at least one-fifth of its volume of water.
2. Solutions of certain alkaloids in propylene glycol can be freely diluted with water without precipitation.
3. Propylene glycol tends to mask the reactions of certain alkaloidal reagents, notably picric acid and tannic acid.
4. Phenolphthalein can be dispensed in solution in therapeutic doses.
5. The halogen salts of sodium and potassium are very soluble in propylene glycol.
6. Dyes are readily soluble. The glycol would therefore be a suitable preservative.
7. Propylene glycol would make a suitable preservative for syrups.
8. It is a solvent for most volatile oils.
9. It may be a suitable menstruum for tinctures (especially senega) owing to its non-volatility, its solvent powers, miscibility with water and alcohol and its preservative action.
10. Propylene glycol considerably retards the volatilization of ethyl nitrite and may conveniently replace alcohol in Sweet Spirit of Nitre."

Ray (28), in a report made in 1935 of some work done on this glycol stated that it dissolves the active constituents of aloes and the tannins in catechu. In a subsequent paper (29), he reported that it was an excellent solvent for vegetable coloring matters and could be used to replace ethylene glycol for this purpose.

Propylene glycol has been used as a solvent for some of the vitamins. An advertisement, which appeared in one of the pharmaceutical journals (30) in 1936, carried the statement that the preparation advertised was a solution of pure crystalline vitamin D in propylene glycol. Data on the treatment of rickets in children with this preparation were reported by Albright, *et al.* (31), in 1937.

Jaros (32), in 1936, reported on the use of propylene glycol as a solvent for benzyl alcohol and diothane in a topical anesthetic for tonsillextirpy.

The successful use of a solution of paraldehyde in propylene glycol as an anesthetic for the relief of pain in labor was reported by Douglas and Peyton (33) in 1937.

Propylene glycol is reported to be used to prepare anhydrous solutions of the barbiturates of sufficient stability to permit of sterilization (34).

Propylene Glycol Stearate.—The stearate of propylene glycol has been found to make an excellent base for suppositories (35). It melts at body temperature, is not irritating and does not leave grease spots.

While it is true that the available literature makes mention of the foregoing, only, as being used for pharmaceutical purposes, it is possible that other sources of

information might disclose additional uses to which these compounds are being put in this field and that some of the other seventeen glycols and glycol derivatives listed in the table are also being used.

At the present time, too little is known about the physiological action of these compounds and of their practical value to predict the nature or extent of their future use in pharmacy. It seems safe to assume however, that the use of those which are found to be non-toxic in the quantities usually used will increase while those which are found to be harmful will be discarded.

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THE ISOLATION AND IDENTIFICATION OF AN ETHER-SOLUBLE ALKALOID IN *COPTIS OCCIDENTALIS*.*,[1]

BY T. D. ROWE.[2]

One of the plants found in abundance in the damp mossy sections of Western Montana is *Coptis occidentalis*, *Ranunculaceæ*. This is a dark green plant averaging about 20 cm. in height, and was first described by Nuttall in 1838 (1). Although small, it is nearly twice as large as its close relative, *Coptis trifolia*, which was official in N. F. V.

In 1873, Gross assayed *C. trifolia* and concluded that a heretofore undiscovered alkaloid was present. This he named Coptine (2). In 1884, Schulze made a quantitative study of *C. trifolia*, and found it to contain 0.012% coptine (3). Since then very little work has been done on either species.

Neither plant seems to have great medicinal value, although in some sections of the west considerable quantities of the dried whole plant of *C. trifolia* are used by the laity in the treatment of various gastrointestinal disorders.

The purposes of this study were: (*a*) to determine the ether-soluble alkaloidal content of *C. occidentalis*; (*b*) to identify this alkaloid by means of qualitative tests. The pharmacology of coptine is yet to be accurately determined.

EXPERIMENTAL.

The major portion of *C. occidentalis* used in this study was collected in October; a small quantity was collected in June. Both portions were air-dried and ground to moderately fine powders.

Extraction with Selective Solvents.—Samples of the whole plant collected in October, weighing about five Gm. each, were extracted by successive extraction in Soxhlet extractors by continuous percolation for 18 hours. The drug was dried to constant weight after the removal of each solvent. The solvents were used in the order listed below; and the following was the average per cent of extractive material obtained:

Solvent.	Per Cent of Extractive.
1. Petroleum Ether	1.0065
2. Ether	1.075
3. Alcohol	23.166
4. Water	11.9215

QUANTITATIVE DETERMINATIONS.

These were made first on four samples each of the rhizomes of the October and June portions. The samples weighed about ten Gm. each. The U. S. P. maceration and aliquot part procedure for proximate assay was followed, using ether and two per cent sulfuric acid as the solvents. The results gave an average of 0.1055% ether-soluble material in the June samples, and 0.1802% in the October portions. Thus the fall samples were shown to contain over 70% more ether-soluble material than the drug collected in the early summer. This was over fourteen times the quantity of alkaloidal material found by Schultz in the whole plant of *C. trifolia*.

Five-gram samples of the leaves were assayed, and yielded 0.133% ether-soluble material. Ten-gram samples of the whole plant were found to contain 0.117%.

Because of the higher content of ether-soluble material found in the rhizomes of the October portion, this was used in most of the experimental work.

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* Presented before the Scientific Section, A. PH. A., Minneapolis meeting, 1938.

[1] Abstract of thesis submitted in partial fulfilment of the degree of Master of Science in Pharmacy, University of Montana. The phyto-chemical work was supervised by Dr. Leon J. Richards, Associate Professor of Pharmacy.

[2] Assistant Professor in Pharmacy, Medical College of Virginia.

QUALITATIVE TESTS.

Qualitative tests showed the material obtained in the quantitative work to be alkaloidal. The tests consisted of adding several alkaloidal precipitants to acid solution samples of the ether-soluble material. Mayer's, Wagner's, Scheibler's and Wormley's reagents were added to separate portions, and a precipitate occurred in each case. Portions of the dried residue obtained in the quantitative determinations were tested for nitrogen by fusing the residue with metallic sodium and testing for the formation of a cyanide. The test was positive on each of several portions. Because of the good results obtained with the precipitants, and with positive nitrogen tests, it was concluded that the ether-soluble material in *C. occidentalis* was alkaloidal.

The residues of the rhizome samples used in the previous work were combined and exhausted with ether. Only one-half of the ether originally used to extract the drug had been removed for the quantitative work, so the remaining ether contained alkaloidal material from the drug. Flasks containing the residues had been well stoppered since the quantitative tests were made, and the drug had been covered with ether. When removed from the drug, the ethereal solutions had a marked purple fluorescence.

The solutions from the residues were combined and divided into two parts, A and B. Solution A was extracted by shaking out in the usual manner, adding portions of two per cent sulfuric acid and then ether, and lastly two per cent sulfuric acid. Solution B was kept unchanged.

Tests were then run on a portion of the acid-water solution obtained from Solution A, with the following results:

1. Mayer's reagent—Definite white precipitate which formed immediately.
2. Wagner's reagent—Slight precipitate, yellowish in color.
3. Picric Acid Solution—Definite white precipitate after 30 seconds.
4. Marmee's Reagent—Indefinite. Slight white precipitate.
5. Scheibler's reagent—Definite white precipitate.
6. Sonnenschein's reagent—Definite yellowish white precipitate.
7. Wormley's reagent—Definite brownish precipitate which formed immediately.
8. Valsar's reagent—Definite white precipitate.
9. Gold Chloride Solution—Precipitate only when heat was applied.
10. Tannic Acid Solution—No reaction, even when heat was applied.

There was a very slight increase in the quantity of each precipitate after standing for five days.

The remaining acid-water solution was allowed to stand for several hours, and the tests applied again. No positive results were obtained. This indicated slow hydrolysis of the alkaloid and for confirmation a fresh acid solution was prepared and tested with the reagents listed above. At twelve noon the results were positive. At five o'clock of the same day the tests were repeated and negative results were obtained. This reaction was noticed several times during the investigation, and indicates that this alkaloid is hydrolyzed slowly by dilute sulfuric acid.

Portions of Solution B were evaporated to dryness on a white "spot" plate and color tests performed. The results were as follows:

1. Concentrated H_2SO_4—Blue color, changing to light pink to darker pink and finally to a very pale lavender.
2. Concentrated HNO_3—Light brown color which did not change.
3. Concentrated NH_4OH—No reaction.
4. Mecke's reagent—Blue color, changing to pink and finally to lavender.
5. Marquis' reagent—Greenish blue color which did not change.
6. Fröhde's reagent—Green color, slowly turning to blue and finally to pink.

The final colors in most of these resembled the color of the fluorescence previously mentioned, and indicate that the fluorescence may be due to the alkaloid present. Confirming results were obtained by repeating the above tests several times.

These "spot plate" tests were run on samples of ether-soluble alkaloid extracted from *Coptis trifolia* and the same results obtained. This indicated that the ether-soluble alkaloids in *C. trifolia* and *C. occidentalis* were the same, *i. e.*, coptine.

These color reactions appear to be characteristic of coptine. Tests tried on berberine gave entirely different reactions, and those listed in Merck's Index f hydrastine separate the latter from the alkaloid studied.

Fluorescent solutions which had been obtained by extracting the drug with ether were tested by allowing acid water to remain in contact with the ether solution for twenty-four hours. The fluorescence disappeared, and alkaloidal tests run on both portions, (1) ether, and (2) two per cent acid solution, gave negative results. This definitely showed that the fluorescence was caused by the alkaloidal material, and that the alkaloid was hydrolyzed by dilute sulfuric acid.

Tests for solubility of the free alkaloid gave the following results:

1. Alcohol—very soluble.
2. Chloroform—soluble.
3. Petroleum ether—slowly soluble; slight heat necessary.
4. Ether—slowly soluble.
5. Two per cent H_2SO_4—very slightly soluble.
6. Water—insoluble; both hot and cold.

FORMATION OF SALTS.

Hydrogen chloride was passed into an ether solution of the alkaloid for an hour. On evaporation of the ether, a white solid appeared. Ether was added and a very small quantity of

Fig. 1.—Coptine + 2% sulfuric acid + 1% picric acid. 16×.

the solid dissolved. Upon addition of water to the remaining part, the material dissolved rapidly. This solution was tested with Mayer's reagent and a precipitate formed immediately. These procedures were repeated as above, and also with slight modifications. Each time a water-soluble salt was obtained which gave characteristic alkaloidal reactions. No fluorescence was noted when the salt was dissolved in water, but when the solution was made alkaline and the alkaloid dissolved in ether, the fluorescence appeared.

Microscopic examination of the hydrochloride showed it to be crystalline in structure. The formation was in mats, composed of small, colorless crystals, monoclinic in structure.

The hydroiodide was formed by adding an ether solution of hydriodic acid to the ether solution of the alkaloid. A precipitate formed immediately, and when tested in the same manner as was the hydrochloride, corresponding results were obtained, indicating that a hydroiodide of coptine was formed. This salt was amorphous and slightly yellow in color. Attempts to form the hydrobromide were unsuccessful.

MICROSCOPIC EXAMINATION OF THE SALTS.

The free alkaloid in ether solution was dissolved in two per cent sulfuric acid, and a drop of this solution placed on each of several slides. A drop of Mayer's reagent was added to one slide, Wagner's to another, Marmee's to a third and Scheibler's to a fourth. A heavy precipi-

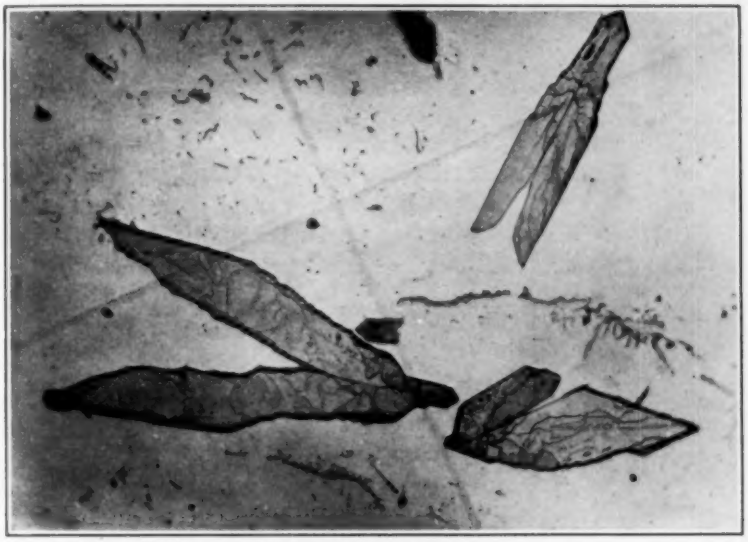

Fig. 2.—Figure 1 enlarged to 62 diameters.

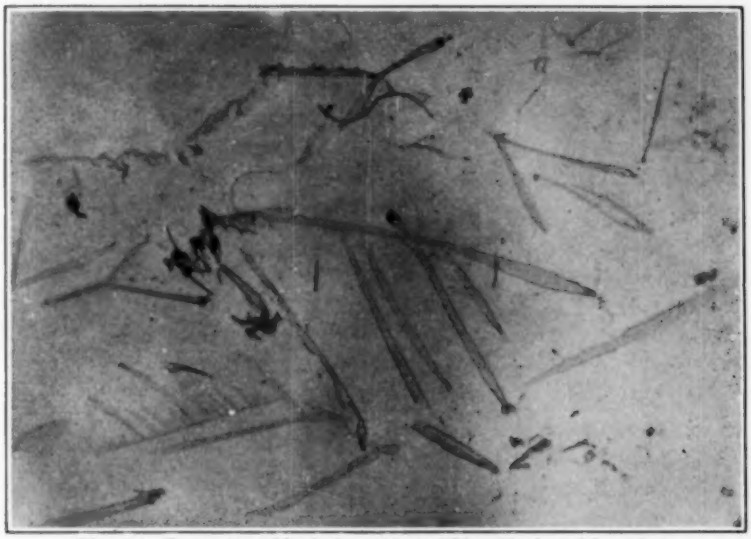

Fig. 3.—Control: 1% picric acid + 2% sulfuric acid. 16×.

tate appeared on each of the slides. To each of four more slides were added the above-named reagents, and a drop of acid solution which contained no alkaloid. The eight slides were covered and allowed to stand for twenty-four hours. Crystals formed on each of the slides. They were then examined in pairs, *i. e.*, Mayer's reagent and alkaloidal salt in acid water was compared with Mayer's reagent and acid water. A study was made of each slide, and the following conclusions drawn: With coptine and 2 per cent sulfuric acid (1) Mayer's, Marmee's and Wagner's reagents

produce an amorphous precipitate; (2) Scheibler's reagent forms clear sheaf crystals. These results were obtained uniformly in a series of comparisons.

Further tests were made using a freshly prepared sample of the alkaloid material, and additional reagents. Of ten reagents used, one per cent picric acid solution gave by far the most

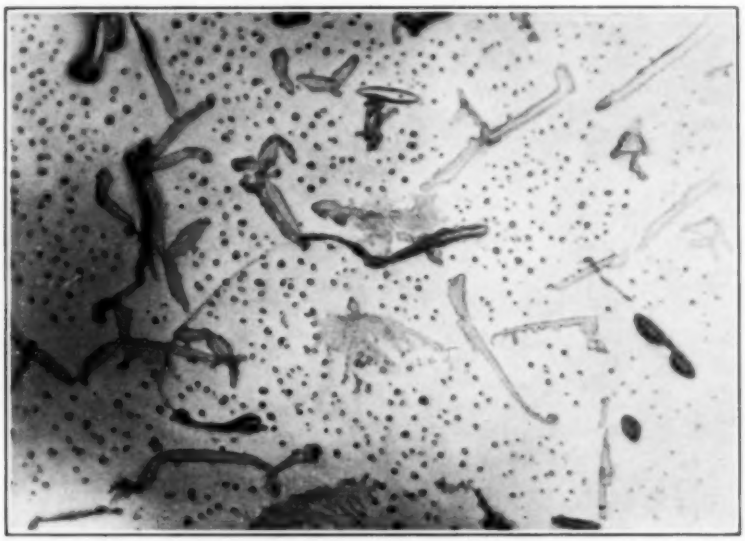

Fig. 4.—Hydrastine + 2% sulfuric acid + 1% picric acid. 16×.

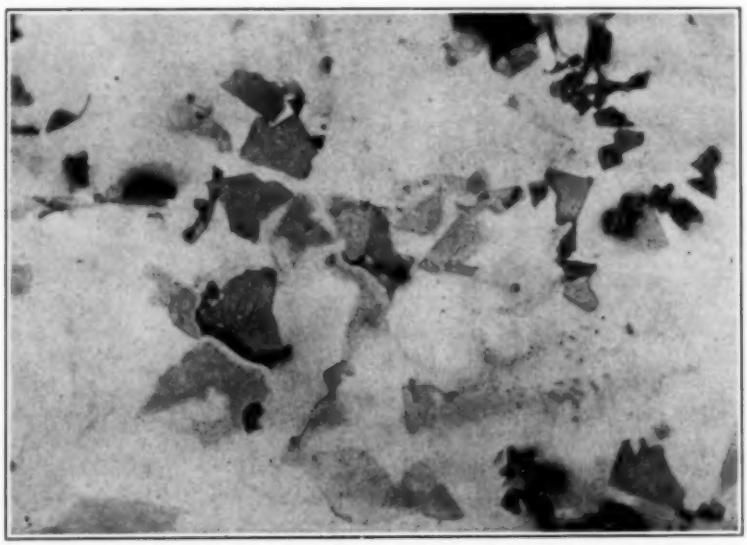

Fig. 5.—Berberine + 2% sulfuric acid + 1% picric acid. 16×.

conclusive results. With the alkaloid material dissolved in H_2SO_4, the picric acid produced definite monoclinic fishtail crystals. They were colorless under ordinary light, but with polarized light they gave striking blue and green colors. The controls of one per cent picric acid solutions with two per cent sulfuric acid contained crystals, but not like the ones obtained with coptine and two per cent sulfuric acid. No fishtails were seen, and the coloring was not as marked under

polarized light. The results can best be compared by a study of the photomicrographs shown in Figs. 1, 2 and 3.

Slides were made of hydrastine in two per cent sulfuric acid, and picric acid solution. The crystals formed were entirely unlike those of coptine and picric acid solution. Photomicrographs of these, and of the crystals obtained with berberine in two per cent sulfuric acid and picric acid, show the marked differences in the three, as seen in Figs. 4 and 5. These tests conclusively set coptine apart from berberine and hydrastine.

SUMMARY AND CONCLUSIONS.

1. *Coptis occidentalis* contains coptine, an ether-soluble alkaloid which is the same as the one found in *Coptis trifolia*. This alkaloid produces a marked purple fluorescence when dissolved in ether solutions.

2. Coptine is hydrolyzed slowly by dilute solutions of sulfuric acid to a form which gives no characteristic alkaloidal tests.

3. Microscopic examinations are practical to identify coptine and to distinguish it from two related alkaloids, hydrastine and berberine; the crystals formed with picric acid solution and coptine in sulfuric acid being particularly efficient for this identification.

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BIOASSAY OF LAXATIVES ON MONKEYS (RHESUS) AND ON LOWER MAMMALIANS (DYEMEAL METHODS).*

BY S. LOEWE.[1]

The potency of many of the laxative preparations in use cannot be measured by chemical methods. Biological procedures must be employed, but the need for dependable bioassay methods for laxatives is unsatisfied.

In 1925, Loewe and Faure (1) devised a "dyemeal" procedure for measuring the passage of the intestinal contents, and applied this procedure to the assay of laxatives. Since that report, these studies have been continued with the objects of improving the bioassay methods implicated in those observations and of finding the most suitable test-animal for laxatives as well as the most appropriate test-function.

In the search for test-animals, our attention was originally directed to the smaller laboratory animals, particularly the albino mouse, which is most appropriate for dyemeal methods. As these studies went on, it became apparent that for many purposes the monkey was superior to all other test-animals. From the numerous manifestations of laxative action, increase in rate of intestinal progression was finally found most appropriate for the dyemeal assays in the mouse, and change in stool consistency for the assay in the monkey. Therefore, the present report on useful routine methods omits all our attempts with other devices of testing the functioning of the intestine, and is restricted to the applications of the dyemeal

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[1] From the Laboratory of the Medical Division, The Montefiore Hospital, New York, N. Y.

methods on smaller rodents and to the method developed for laxative bioassay in the rhesus monkey.

A. DYEMEAL METHODS.

Principle.—The underlying principle of the dyemeal methods is to measure the rate of progression of intestinal contents. A dyemeal is employed to provide an easily traceable material. The rate of progression is measured in one of two ways, either by recording the time necessary for the meal to traverse a given distance ("time method") or by measuring the distance traversed in a given time ("distance method"). In either case, a precise starting time is secured by administering the dyemeal through a stomach tube. In the time method, the distance employed is that from the pyloric sphincter to the anus, the arrival of the dyemeal at the latter point being indicated by the evacuation of the first dyed stool. In the "distance method" the time selected for killing the animals was either 120 or 160 minutes, and the distance measured immediately after death was that from the pyloric sphincter to the most advanced position of the dyemeal. The "distance method" is the procedure of choice because the "time method" involves a second variable, namely, the defecation reflex. It has been found that a considerable laxative effect can be masked by delayed defecation.

Technique.—The albino mouse is the species of preference. The meal consists of a non-absorbable dye. No significant difference was found between India ink, colloidal charcoal and carmine. For the purpose of decreasing the considerable individual variation in intestinal motility in mice, the meal may contain a mucilage (1% to 2% salep or tragacanth, or 10% to 20% gum acacia). The test dose is added to the dyemeal, if the drug acts sufficiently rapid. Otherwise the drug is administered 30 to 120 minutes prior to the dyemeal, generally by stomach tube. The total volume of the dyemeal is 0.3 cc. Each dose of the test substance is given to a series of at least 7, preferably 10 to 15, animals. Two control series are run, one consisting of a group of mice receiving only the dyemeal, and another group receiving suitable doses of an appropriate reference preparation.

Interpretation of Results.—The results are expressed in terms of (relative) potency, *i. e.*, the ratio of equi-effective doses of test substance (T) and reference preparation (R): R/T. In the "time method" those doses are equi-effective which cause an equal shortening of defecation time; in the "distance method," those doses which allow the dye to reach an equal position in the large intestine.

Applications and Restrictions of the Dyemeal Methods.—The dyemeal methods fundamentally can be employed with any species of laboratory animals. In addition to mice, rats (2) and guinea pigs have been used. These two species, however, have no advantage over the mouse; the mouse has the advantage of low cost and small absolute dose. The susceptibility of all these animals to laxatives, nevertheless, is rather low in comparison to humans; large doses relative to body weight must be employed, and rodents, as all the species below the primates, are insensitive to several laxatives effective in man. Those drugs which have been tested in mice are the following, in order of decreasing effectiveness: physostigmine, cholin esters, castor oil, salines, anthraquinones, colocynth, calomel, diphenolisatines and phthaleins.

B. MONKEY METHOD.[1]

I. Principle.

Williams, Abramowitz and Killian (1933) (3) showed that phenolphthalein is an effective laxative for the rhesus monkey (*Simia rhesus*). The method described here resulted from a continuation of the work of these authors. To date, 4500 experiments have been performed on 128 monkeys.

Early in the course of this study, it became obvious that the susceptibility to laxatives varies greatly in different monkeys, as well as in the same animal at different times. For example, the average effective doses as determined for individual monkeys may differ as much as ±98% from the group average. Also, for a particular monkey, at different times variations may occur in the response to doses extending over a range of ±60% of the average dose for that animal.

[1] These monkey experiments have been sponsored by Ex-Lax, Inc., Brooklyn, N. Y.

The details of susceptibility of the monkey which will be reported in a separate communication are necessarily of great significance for the development of any procedure for assaying unknown laxatives. Any bioassay has the purpose of determining the dosage relation between the test preparation and a reference preparation. This relation is usually expressed in terms of (relative) potency, *i. e.*, in the ratio R/T (see page 428) of equi-effective doses of the two preparations. In the rhesus monkey, because of the above individual and group variations, equi-effectiveness offers no definite measure of potency. It is much more conclusive to consider the relation of inequi-effective doses in a procedure of "bioassay by approximation" (4). In applying this procedure to the rhesus monkey, the following principles were adopted:

1. Different preparations may only be compared with each other on the same test-animal. The average dose for an entire group is of no value.

2. Only "effectiveness" and "ineffectiveness" may be considered in evaluating the laxative response. The finer grades of intensity of action are observed, but not considered too significant, because of the fluctuating susceptibility.

3. Ineffective doses of the test preparation may only be referred to effective doses of the reference preparations, and effective test doses only to ineffective reference doses. With the aid of these cross-comparisons, from which border values of maximum and minimum potency are obtained, the range of potency may be determined by approximation.

4. Only animals in which the range of reference has been carefully determined may be used for evaluations. The accuracy of the assay depends upon thorough "calibration" of the animal with respect to the reference preparation.

II. Care of the Experimental Animals.

Animals.—Adult animals (1500 to 5500 Gm.) are used. Weight and temperature are biweekly controlled. Sex has been found to be relatively unimportant. The number of stock animals ranged from 45 to 60.

Housing.—The monkey house is a glass-brick building with ample daylight and air-conditioned to an average of 75° F. Each animal is placed in an individual all-round-metal screen cage measuring 10 cubic feet. Interchangeable screen-covered metal pans allow the stools to be collected, and aid in keeping the cages clean. Cages are placed on wheel stands to facilitate cleansing and exposing the animals to open air and sunlight.

TABLE I.—DIET.

	Monday.	Tuesday.	Wednesday.	Thursday.	Friday.	Saturday.	Sunday.
Forenoon:	One slice of wheat bread and butter, and:					2 Slices of wheat bread and butter	
	1 orange	1/2 apple	1 orange	1/2 apple	1 orange		
Afternoon:	100 Gm. lettuce, 100 Gm. boiled potato, 1 hard boiled egg	100 cc. milk, 100 Gm. carrots, 100 Gm. boiled potato	100 Gm. lettuce, 1/2 cup "monkey food," 100 Gm. boiled potato	100 Gm. raw or cooked oats or rice, 100 Gm. tomato pulp with bone- and blood-meal	Same as on Monday	100 Gm. carrots, 100 cc milk	100 Gm. lettuce, 1 apple

Diet.—Two meals are fed daily, 9:30 A.M. and 4:30 P.M. The diet schedule is shown in Table I. Water is offered liberally.

Stool Records.—Records are kept of the number of stools per day and of the stool characteristics, the latter in numerical designations—lacking (0), solid (2), medium (4), soft (6), liquid (8) or intermediate between these (3, 5 or 7, respectively)—and summarized for each test monkey in a continual "stool curve" (Fig. 1). Monkeys fed the above diet consistently passed "hard" (2) stools.

III. Technique of Bioassays.

Administration of Laxatives.—Only animals with hard stools are used. Doses are weighed individually with a maximum error of 1.5%. Most laxatives are easily fed as powder or solution, by introducing them into a slice of banana, apple or potato. The dose is usually administered before the afternoon meal, and must be consumed without delay.

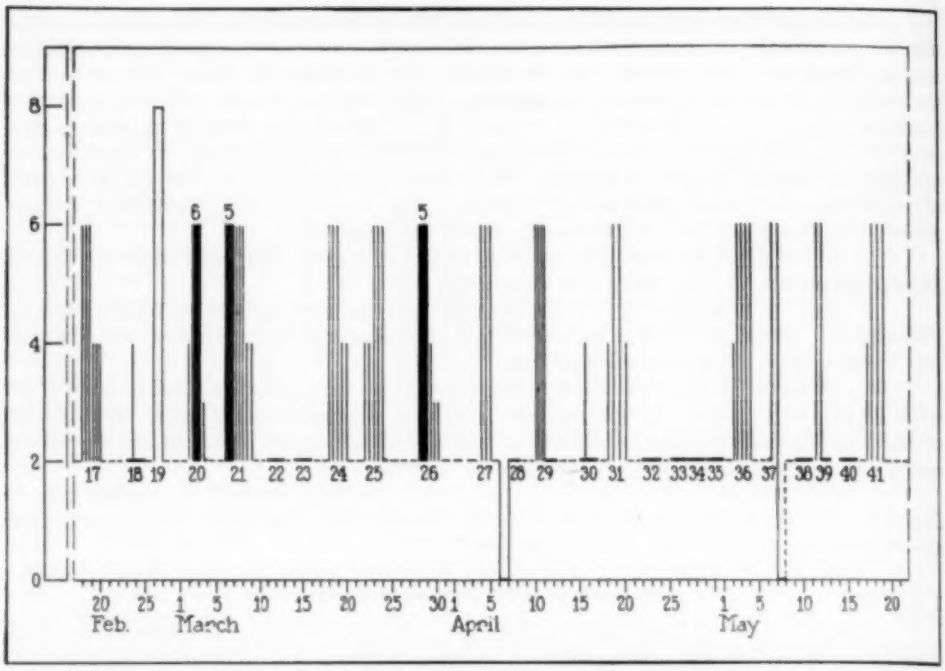

Fig. 1.—Part of Stool Curve of monkey No. 352.—Abscissa: calendar days; ordinate: stool consistency (see text for explanation of figures). Figures at ordinate level 2 are Prot. Nrs. of laxative experiments performed; figures at ordinate level 6: number of stools on particular day.

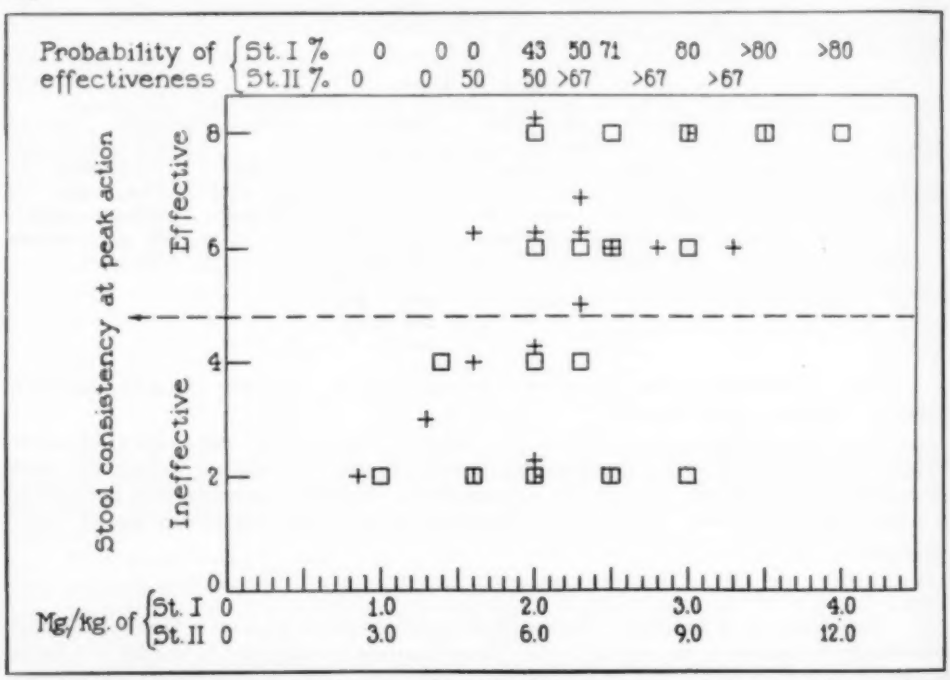

Fig. 2.—Calibration Graph of monkey No. 282.—□ = one, ⊡ = two, ⊞ = three, ⊟ = four experiments with reference preparation No. I ("St. I"); + = single experiments with reference preparation No. II ("St. II").

Determining the Laxative Action.—The action is recorded in the "stool curve" (see Fig. 1). The final result is determined by the stool consistency during the period of greatest deviation of the stools from the normal, results 0 to 4 are designated as "ineffective," 5 to 8 as "effective."

Evaluating Individual Susceptibility (Calibration of Animals).—For a precise calibration of each monkey, it is necessary to examine a wide range of doses of an appropriate reference substance repeatedly before and after examining the unknown laxative. When assaying laxatives from various chemical classes, a well-defined preparation from any of these, when assaying different lots of the same laxative, a single lot of suitable potency is selected as the reference preparation. Our animals were calibrated simultaneously with a highly purified U. S. P. phenolphthalein, a commercial phenolphthalein and a pure diacetyldiphenolisatine. Monkeys, when satisfactorily calibrated, have an individual record of 22 to 56 calibration experiments which is summarized in the form of a "calibration graph" with an abscissa of mg. per Kg. for the reference preparations, and an ordinate of the responses recorded by stool consistency, as in Fig. 2.

The task of calibration is to ascertain the "Maximum Ineffective Dose," L, and the "Minimum Effective Dose," H, of the reference preparation, valid for the particular monkey pending revision through subsequent re-calibration. L is the dose with an incidence of not more than 10% of positive, H that with not more than 10% negative responses; if the number of experiments is insufficient for direct determination, either of these doses may be calculated by interpolation.

Performance of the Bioassay.—Administer orally graduated doses of the test preparation to 7 to 10 well-calibrated monkeys. Observe subsequent evacuations for at least 2 days, and determine if the dose was "effective" or "ineffective" (see above). Calculate for each single experiment either the maximum potency by dividing the reference dose, H, of the same animal by the ineffective test dose, d; or the minimum potency by dividing the reference dose, L, by the effective test dose, D. Group each of these two series of potency values in arithmetical progression, and find the potency as the mean value between the lowest maximum (H/d) and the highest minimum (L/D) figure (4). If the range between these two values varies by more than $\pm 15\%$ of its mean value, or is determined by less than four experiments, perform an additional series of tests with appropriate doses.

For the sake of comparison, many of the bioassays performed have also been calculated by referring the test dose to a "Reference Standard Dose," $R_{50} = {}^1/_2 (L + H)$, of the same animal. The results reached by this procedure were naturally found to be less conclusive, because of the considerable individual variation. Any type of "Unit Dose" is an inadequate reference dose unless the validity of this figure is defined by considering the range of deviation (compare Fig. 2).

Applications and Advantages of the Monkey Method.—The method presented here has been found applicable to all three purposes of bioassay, namely, to compare active principles from different pharmacological classes, different preparations of the same active principle or different lots of the same preparation. Laxatives from the following classes have been comparatively evaluated with phenolphthalein and diacetyldiphenolisatine as reference substances: salines, anthraquinones, isatines and phthaleins. Various preparations of the same active principle have been compared with each other, *e. g.*, extracts from senna and esters from the isatine and phthalein groups. Finally, the differences in potency between batches of the same preparations have been determined, *e. g.*, of diphenolisatine-esters and phenolphthalein.

When assays of the same test substance were repeated after varying intervals with the use of different monkeys, the results always agreed within a range of $\pm 15\%$. This is a degree of reproducibility rarely exceeded in any bioassay method.

The rhesus monkey responded to all the numerous laxatives tested. The ease with which the rhesus can be used as a test animal for phenolphthalein is a decided advantage in the pharmacological investigation of this drug hitherto hampered by the lack of an appropriate test-animal.

The monkey is one of the very few animals which is similar to humans in its responses to laxatives in doses comparable to those used clinically. This is illustrated by the following example of parallel experiments on the rhesus and on humans, details of which will be reported in a separate paper:

Four laxatives (I, II, III and IV) of different potency were prepared, all containing phenolphthalein. They were first carefully assayed in the monkey. Four groups of healthy human volunteers were used, each consisting of between 272 and 593 individuals. As can be seen in

Table II, the figures for relative potencies obtained by assay on the monkey show a surprising correlation with those found by human assay.

TABLE II.

Potencies of four test-substances I, II, III and IV in the rhesus monkey and in healthy humans (number of "watery" responses per hundred "soft" responses). Relative Potencies as referred to that of substance I = 1.0.

Test-Substance No.	I.	II.	III.	IV.
Relative potency found:				
(*a*) in the monkey:	1.00	1.74	2.22	2.67
(*b*) in humans:	1.00	1.70	1.90	3.50

SUMMARY.

1. Two techniques for bioassaying laxatives are described: (*a*) the dyemeal methods on smaller laboratory animals; (*b*) a method which uses the monkey as test-animal. The advantages and restrictions of the dyemeal methods are briefly discussed.

2. A method of "bioassay through approximation" is recommended for the evaluation of laxatives. The rhesus monkey is the test-animal, and the method is based upon a thorough study of the individual and group variations in the susceptibility in this species.

3. In more than 4500 experiments on 128 monkeys, the method was found valuable for the bioassay of laxatives from different pharmacological groups as well as for comparing the potency of various preparations of the same active principle and different batches of the same preparation. The error of the method is not over ±15% and usually less.

4. The method was found to be far superior to any existing bioassay method for laxatives. The monkey manifests susceptibility to a large number of laxatives and its sensitivity to these is comparable to that of humans. By assaying four different laxative preparations on monkeys and on several thousand healthy humans, the same values of relative potency were found.

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PHARMACEUTICAL SOCIETY OF GREAT BRITAIN.

The 98th annual meeting of the Pharmaceutical Society of Great Britain was held May 17, 1939, President Thomas Guthrie presiding. Under Public Services he referred to the efforts of the Society to secure adequate pharmaceutical services and discussed the actions of the members in air raid precautions.

The President discussed his membership during the past twenty-three years, in the Council, and stated that he is now retiring as a member. A tribute was paid him.

An important discussion ensued, relating to students of Pharmacy and conscription; it was the opinion that students should not be taken from their last year of study for six months; the matter has been discussed with the Ministry of Labor, but the decision of the latter has not been received.—From the *Pharmaceutical Journal*.

THE CHEMICAL EXAMINATION OF ESSENTIAL OILS FROM *ABIES AMABILIS* AND *GRANDIS*.*

BY MALCOLM S. TRUPP[1] AND LOUIS FISCHER.[2]

PART I.

Abies amabilis (Forbes), commonly known as "white fir" or "silver fir," is a coniferous tree growing abundantly in dense forests on the western slopes of the Cascade Mountains, preferably on benches or flats or on the lower slopes of canyons where excellent soil drainage is available and at altitudes ranging from 1000 to 6000 feet above sea level. This tree attains a height of from 100 to 150 feet and varies between 3 and 5 feet in diameter.

A superficial study of the volatile oil from the bark of *Abies amabilis* was conducted by Rabak (1), who determined a few physical constants and stated that the oil contained lævo-pinene and probably lævo-limonene.

EXPERIMENTAL.

Two lots of bark, collected in December 1936 in the vicinity of Mt. Rainier National Park, Washington, were subjected to steam distillation. From a total of 316 pounds of fresh bark there were obtained 850 cc. or 1.60 pounds of oil which represented a yield of 0.50 per cent. The dry oil, faintly yellow in color, possessed a slight aromatic odor.

The physical constants, determined in the usual manner, were as follows: d_{20} 0.8576; n_D^{20} 1.4772; $[\alpha]_D^{20}$ −10.52°; saponification number 2.22; acid number 0.26; ester number 1.96; and acetyl number 6.18.

Free Acids: Acetic Acid.—Five hundred cubic centimeters of the oil were extracted with 5 per cent sodium carbonate solution. The basic solution, upon acidification and extraction with ether, furnished 0.075 Gm. of acidic material, representing a yield of 0.017 per cent. This material, after mixing with hot water, was filtered. The filtrate, neutralized with calcium hydroxide and evaporated to dryness, was extracted with alcohol. The residue, remaining, gave the usual tests for acetic acid. Although traces of acidic materials insoluble in hot water were left on the filter, insufficient evidence was obtained for their identification.

Phenols.—Extraction of the oil with 5 per cent potassium hydroxide solution and subsequent treatment of the acidified liquid with ether yielded 0.035 Gm. of oily residue, representing 0.008 per cent of the oil by weight. A solution of this material in alcohol produced a purple color with ferric chloride solution. No identification was possible, since several phenols give similar color reactions.

Aldehydes.—Because the oil gave reduction tests with Tollen's and Schiff's reagents, it was extracted with a saturated solution of sodium bisulfite. This solution, decomposed with sodium carbonate and extracted with ether, yielded a negligible quantity of oily substance. Extremely small traces of aldehyde materials were present, although no satisfactory identifications could be made.

Fractionation.—The remaining oil, free from acids, phenols and aldehydes was dried, filtered and subjected to fractional distillation. The liquid, boiling below 100° C. at reduced pressure, was fractionated repeatedly until the following fractions were obtained:

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[1] Fellow, College of Pharmacy, University of Washington.

[2] This paper was directed jointly by Louis Fischer, College of Pharmacy, University of Washington, and Russell A. Cain, Sharp and Dohme Laboratories.

Fraction No.	Boiling Point, ° C.	Volume, Cc.	Per Cent by Volume.	$[\alpha]_D^{20}$.	d_{20}.	n_D^{20}.
I	157–162	19.0	3.80	−13.48°	0.8993	1.4898
II	163–173	339.0	67.80	−11.48°	0.8597	1.4891
III	174–178	2.2	0.44	.....	.....	.....
IV	178–208	2.0	0.40	.....	.....	.....

Lævo-Alpha-Pinene.—A nitrosochloride was prepared from Fraction I according to the method of Wallach (2). This derivative, purified by precipitation from a chloroform solution with methyl alcohol, was found to melt at 109° C. Admixture with a nitrosochloride prepared from turpentine oil caused no reduction in the melting point.

For further confirmation of this constituent, five cc. of this fraction were oxidized to pinonic acid with concentrated potassium permanganate solution following the method of Parry (3). A semicarbazone prepared from the pinonic acid after recrystallization from hot alcohol melted at 204° C. The results obtained indicate the above fraction to be composed principally of alpha-pinene. The above derivatives were also obtained from Fraction II, indicating the presence of appreciable quantities of alpha-pinene.

Lævo-Beta-Pinene.—A portion of Fraction II was oxidized to sodium nopinate with concentrated permanganate solution in the presence of sodium hydroxide, according to the method of Wallach (4). An acidified solution of sodium nopinate was extracted with ether. The nopinic acid, after crystallization from the solvent, melted at 124–125° C. Since only small quantities of nopinic acid were obtainable and the preparation of other derivatives was dependent upon this substance, one may conclude that limited amounts of beta-pinene are present in Fraction II as indicated by the above results.

Lævo-Beta-Phellandrene.—A solid nitrite was prepared from Fraction II using the method of Wallach and Gildemeister (5). After purification by precipitation from a cooled acetone solution with water, this derivative was found to melt at 98° C. This corresponds to the melting point of beta-phellandrene-beta-nitrite.

For further identification a cooled portion of the above fraction was oxidized with potassium permanganate solution according to Wallach's method (6). After removal of unoxidized materials from the concentrated aqueous solution, a glycol was extracted with chloroform. This substance, upon dehydration with 50 per cent sulfuric acid and subsequent steam distillation, furnished tetrahydrocuminic aldehyde. A semicarbazone, prepared from the latter and precipitated from acetone, melted at 202° C. The above derivatives indicated the presence of appreciable amounts of beta-phellandrene in Fraction II. In a similar manner, beta-phellandrene was also found to be present in Fraction IV.

Combined Acids: Acetic Acid.—The oil distilling above 100° C. at reduced pressure was saponified with alcoholic potassium hydroxide. After removal of the alcohol, the aqueous washings were acidified and extracted with ether. A total of 0.883 Gm., representing a yield of 0.21 per cent of acidic material, was obtained. The aqueous distillate of this mixture, after steam distillation, was neutralized with calcium hydroxide solution, evaporated to dryness and extracted with alcohol. The usual qualitative tests were obtained for acetic acid. No non-volatile acids could be identified although they represented the greater portion of the acid residue.

Fractionation of the High-Boiling Portion.—The oily portion, freed of combined acids, represented 2.55 per cent of the original volume. After several refractionations at reduced pressure the following fractions were obtained:

Fraction No.	Boiling Point (24 mm.), ° C.	Volume, Cc.	Per Cent by Volume.	Color.
I	110–114	1.0	0.20	Colorless
II	150–157	1.0	0.20	Yellow
III	184–208	2.0	0.40	Orange
	Residue	...	....	Brown

Although Fractions I and II were thought to contain alcohols, none could be identified. No constituents could be identified in Fraction III which was slightly decomposed.

SUMMARY.

The fresh bark yielded 0.50 per cent of essential oil, containing 72.4 per cent of terpenes and 2.55 per cent of high boiling liquid. The terpenes present were mainly lævo-alpha-pinene and lævo-beta-phellandrene with smaller quantities of lævo-beta-pinene. Traces of free acetic acids, phenols and aldehydes were present. Only acetic acid could be identified in the combined state although some non-volatile acids were undoubtedly present.

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PART II.

In the above it was stated that the oil from the bark of *Abies amabilis* (Forbes) had been superficially examined. However, a complete survey of the literature revealed that, up to the present time, no attempts had been made to investigate the oil from the leaves of this tree.

EXPERIMENTAL.

The small twigs with leaves attached, collected between November 1936 and December 1937 from trees located in the vicinity of Mt. Rainier National Park, Washington, were distilled with steam. A total of 889.75 pounds of fresh leaves and twigs yielded 0.713 pound of volatile oil, corresponding to 0.08 per cent. The oil was colorless and possessed an odor similar to that of turpentine oil.

The physical and chemical constants, determined in the usual manner, were as follows: $[\alpha]_D^{20}$ −3.79°; d_{20} 0.8574; n_D^{20} 1.4770; saponification number 4.63; acid number 0.80; ester number 3.83; and acetyl number 12.29.

Free Acids.—The free acids, removed from 351 cc. of the oil with 5 per cent sodium carbonate solution, were liberated by the addition of acid to the alkaline liquid and extracted with ether. A total of 0.06 Gm. of brown, syrupy, acidic residue was obtained, representing 0.02 per cent of the original oil by weight. A portion of the residue, neutralized with calcium hydroxide, produced an ester-like odor in the presence of ethyl alcohol and sulfuric acid. However, after the application of the usual methods of analysis no individual acids could be identified.

Phenols.—The phenolic substances, extracted from the oil with 5 per cent potassium hydroxide solution, were liberated from the alkaline solution by acidification with sulfuric acid and extracted with ether. A small amount of viscous material, possessing a tarry odor, was obtained weighing 0.0995 Gm. and representing a yield of 0.03 per cent. A portion of this substance in aqueous solution produced a purple color with ferric chloride and in alcoholic solution a reddish brown color, indicating the presence of phenols. Since these color reactions are common to several phenols no identification was possible.

Aldehydes.—Because the oil slowly reduced Tollen's reagent and restored the color to Schiff's reagent, the aldehydes were removed from it by shaking with a saturated solution of sodium bisulfite. This solution was then decomposed with a warm, saturated solution of sodium carbonate and extracted with ether. Upon recovery of the ether, a small quantity of oily residue remained, weighing 0.0503 Gm. and representing a yield of 0.02 per cent. A semicarbazone was formed with this material but it was insufficient in quantity to perform a melting point determination.

Fractionation.—A total of 330 cc. of the dried oil, free from acids, phenols and aldehydes, was separated into a low- and high-boiling portion by several distillations. The low-boiling liquid, distilling from 60–66° C. at about 14 millimeters, was repeatedly refractionated at reduced and atmospheric pressure until the following fractions were obtained:

Fraction No.	Boiling Point (763.8 mm.), ° C.	Volume, Cc.	Per Cent by Volume.	d_{20}.	$[\alpha]_D^{20}$.	n_D^{20}.
I	161–167	127.0	38.48	0.8562	−2.04°	1.4735
II	167–171	124.0	37.57	0.8532	−3.07°	1.4761
III	173–186	10.0	3.03	0.8580	−9.90°	1.4804
	Residue	7.0	2.12	.....	.....	.....

Lævo-Alpha-Pinene.—A nitrosochloride, prepared according to the method of Ehestädt (1) from the fraction distilling between 161–167° C., was purified by precipitation from a cooled chloroform solution with methyl alcohol. This derivative melted at 110° C. Depending on the purity of this compound, considerable variation (103–115° C.) in the melting points have been observed (2).

The more stable nitrolbenzylamine derivative was prepared from the nitrosochloride by Wallach's method (3). The dry crystals, which had been precipitated from water and washed with alcohol, were found to melt at 122–123° C., the true melting point for the pure substance.

To further prove the presence of alpha-pinene, a portion of the above fraction was oxidized to pinonic acid with potassium permanganate, following the method of Parry (4). The semicarbazone of the acid was prepared and, after recrystallization from hot alcohol, melted at 204.5° C. The results show the above fraction to consist chiefly of alpha-pinene. Alpha-pinene was found to be present in Fraction II by similar oxidation methods.

Lævo-Beta-Pinene.—A portion of Fraction I yielded nopinic acid when oxidized with an alkaline solution of potassium permanganate using Wallach's method (5). The acid after recrystallization from an ether-benzene solution melted at 124–125° C. Since this melting point was near that of the pure compound, it was assumed that small amounts of beta-pinene were present in Fraction I.

Lævo-Beta-Phellandrene.—A solid nitrite was prepared from a portion of Fraction III according to the method of Wallach and Gildemeister (6). This derivative, after purification by recrystallization from a cooled aqueous acetone solution, melted at 102.5° C. corresponding to the pure compound.

For further identification, a nitrosochloride was prepared from a portion of the fraction according to the method of Ehestädt (1). This substance, when purified by precipitation from a chloroform solution with methyl alcohol, melted at 108° C. Although this melting point does not agree exactly with that of the pure compound, the results point to the possible presence of small quantities of beta-phellandrene in this fraction.

SAPONIFICATION AND DISTILLATION OF THE HIGH-BOILING LIQUID.

The high-boiling liquid after saponification was washed free of salts and excess alkali, dried and fractionally distilled at reduced pressure. The following portions were obtained after repeated refractionations:

Fraction No.	Boiling Point (14 mm.), ° C.	Volume, Cc.	Per Cent by Volume.	d_{20}.	$[\alpha]_D^{20}$.	n_D^{20}.
I	71–90	9.3	2.81	0.8621	−5.41°*	1.4812
II	90–110	2.0	0.60	0.8903	−7.64°	1.4872
III	110–130	2.1	0.63	0.9077	−6.16°	1.4890
IV	130–147	4.7	1.42	0.9101	1.45°	1.4949
	Residue	..	..	..	..	..

* In chloroform.

Although either phellandrene or terpinene was suspected in Fraction I, no solid derivatives could be prepared for identification.

All efforts to identify sesquiterpenes or alcohols in Fractions II and III proved to be negative, neither could any trace of sesquiterpenes be distinguished in the fourth fraction.

Combined Acids: Acetic Acid.—After saponification of the high-boiling liquid, the alkaline washings were acidified with dilute sulfuric acid and steam-distilled. The aqueous distillate containing no insoluble volatile material was neutralized with calcium hydroxide solution, evaporated to dryness and extracted with alcohol. The residue remaining gave the usual tests for acetic acid. Only traces of other volatile acids seemed to be present.

Upon removal of the solvent, from an ether extract of the liquid remaining in the distillation flask, a brown residue was obtained. Neutralized portions of this residue formed insoluble salts with silver nitrate, but the silver content of each portion varied too greatly for accurate identification.

SUMMARY.

The fresh leaves and twigs of *Abies amabilis* yielded 0.08 per cent of volatile oil which contained traces of free acids, phenols and aldehydes. The low-boiling portion consisted of 81.21 per cent of terpenes; alpha-pinene being present in the largest quantities with smaller amounts of beta-pinene and beta-phellandrene. No sesquiterpenes or alcohols could be identified in the high-boiling liquid which represented 12.42 per cent of the original oil. Acetic acid was found to be the principal combined acid.

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PART III.

Abies grandis (Lindley), commonly known as the grand or white fir, is a tall, straight tree growing to a height of from 150 to 275 feet and is 3 to 4 feet in diameter. It may be found growing from sea level to an altitude of 3000 feet or more, usually preferring low benches or flats where excellent soil drainage is available.

The volatile oil from the leaves and twigs of this tree was recently investigated by Charles Schwartz, Jr. (1), who determined the physical constants of the oil and found it to contain the terpenes alpha-pinene, beta-pinene, beta-phellandrene and camphene. Analysis also indicated the presence of borneol, as bornyl acetate, and traces of free acids and phenols.

The volatile oil, obtained from the bark of *Abies grandis*, has not been previously examined.

EXPERIMENTAL.

The bark from the white fir was collected in May 1937 from trees growing in the vicinity of Enumclaw, Washington. The fresh bark weighing 576 pounds was steam-distilled and produced 981.95 Gm. of oil which represented a yield of 0.37 per cent.

The physical and chemical constants were determined in the usual manner and were as follows: $[\alpha]_D^{20}$ −32.83°; d_{20} 0.8935; n_D^{20} 1.4917; saponification number 54.57; acid number 0.39; ester number 54.18; and acetyl number 8.85; total esters (calculated as bornyl acetate) 18.90; total alcohols (calculated as borneol) 18.01; combined alcohols (calculated as borneol) 14.83; and free alcohols (calculated as borneol) 3.18.

Free Acids.—Extraction of 500 cc. of the oil with a 5 per cent sodium carbonate solution and subsequent treatment of the acidified aqueous solution with ether yielded 0.2675 Gm. of yellow residue, which represented 0.05 per cent of the oil. The residue was distilled with steam, the distillate neutralized with calcium hydroxide, evaporated to dryness and extracted with alcohol. The residual material was found to contain acetic acid upon application of the usual qualitative tests. Although small amounts of the other lower fatty acids possibly were present none could be identified.

Phenols.—The oil was then treated with a 5 per cent potassium hydroxide solution, acidified and extracted with ether. A yield of 0.0943 Gm. of phenolic materials representing 0.02 per cent, was obtained. The residue was a viscous, reddish brown liquid and possessed a faint musty-like odor. An aqueous solution of this substance gave a purple color with ferric chloride indicating the presence of phenols. Another portion of the residue with phenylisocyanate produced a phenylurethane, which melted at 49–50° C. A review of the known phenylurethanes gave no clue to the identity of this material and insufficient substance was at hand for further investigation.

Aldehydes.—Since the oil slowly reduced Tollen's and Schiff's reagents, it was extracted with a saturated solution of sodium bisulfite. The latter solution was then decomposed with dilute sulfuric acid and extracted with ether. The oily residue so obtained was too small for further investigation.

Fractionation.—Four hundred and sixty-eight cubic centimeters of oil, free from acids, phenols and aldehydes, were separated into a low- and high-boiling portion by fractional distillation at reduced pressure. After repeated refractionations of the low-boiling liquid at reduced and finally at atmospheric pressure, the following fractions were obtained:

Fraction No.	Boiling Point (748.6 mm.), ° C.	Volume, Cc.	Per Cent by Volume.	$[\alpha]_D^{20}$.	d_{20}.	n_D^{20}.
I	159–162	92.0	19.65	−39.40°	0.8692	1.4847
II	162–165	89.0	19.44	−32.77°	0.8729	1.4887
III	165–172	72.0	15.38	−33.05°	0.8637	1.4896
IV	172–179	18.0	3.84	−32.49°	0.8820	1.4910
V	185–205	7.0	1.49	.....	0.9248	1.4856

Lævo-Alpha-Pinene.—A solid chlorohydrate derivative was obtained when dry hydrogen chloride gas was passed through a cooled portion of Fraction I. After several recrystallizations from alcohol, the derivative was dried and found to melt at 124–125° C.

For further identification, another portion of this fraction was oxidized to pinonic acid with concentrated potassium permanganate solution using the method of Parry (2). A semicarbazone derivative, prepared from the pinonic acid, was purified by recrystallization from hot alcohol and after drying melted at 204–205° C. The derivatives, formed, prove the main constituent of Fraction I to be alpha-pinene.

Lævo-Beta-Pinene.—A portion of Fraction II was examined for beta-pinene by oxidation with potassium permanganate in the presence of sodium hydroxide according to the method of Wallach (3). The principal oxidation product, sodium nopinate, was then acidified with dilute sulfuric acid and extracted with ether. Evaporation of the solvent yielded long, colorless needle-like crystals of nopinic acid which melted at 126–126.5° C. Admixture with a known nopinic acid produced no depression in the melting point.

Beta-pinene was further identified by the oxidation of the nopinic acid with one per cent potassium permanganate solution to form the ketone nopinone. A semicarbazone of nopinone, recrystallized from alcohol, was found to melt at 188–190° C. From the amounts of the derivatives prepared, one can conclude that beta-pinene is the chief component of Fraction II. In a similar manner, Fraction III was found to contain beta-pinene.

Lævo Camphene.—A portion of Fraction II, boiling from 162–165° C., was hydrated to isobornyl acetate with glacial acetic acid following the method of Bertram and Walbaum (4). After saponification of the isobornyl acetate, the isoborneol was precipitated by throwing the mixture into water. The isoborneol was obtained in a pure state after absorption of the excess oily material on a porous plate. Recrystallized from alcohol, it melted at 208° C.

Although no phenylurethane could be formed for further identification, the results obtained would seem to indicate the presence of appreciable quantities of camphene in Fraction II.

Lævo-Beta-Phellandrene.—A solid nitrite derivative, prepared from a portion of Fraction III according to the method of Wallach and Gildemeister (5), was purified by recrystallization from a cooled, diluted acetone solution. The resulting crystals of beta-phellandrene-alpha-nitrite, after drying, melted at 104° C.

For further identification, another portion of the fraction was oxidized to a glycol with one per cent potassium permanganate solution using the method of Wallach (6). The resulting glycol, obtained by extraction from the aqueous liquid with chloroform, was steam-distilled in the presence of 50 per cent sulfuric acid. A semicarbazone of tetrahydrocuminic aldehyde was formed from the distillate and, after recrystallization from methyl alcohol, melted at 204° C.

Similar results were obtained with Fraction IV indicating that beta-phellandrene was present in each fraction.

Examination of the High-Boiling Liquid.—The high-boiling portion of the oil, measuring 158 cc. and representing a third of the original volume, was saponified with alcoholic potassium hydroxide. After the alcohol was removed by distillation, the oily material was washed free of salts, dried, filtered and subjected to fractional distillation at reduced pressure. Fraction I proved to be a camphor-like solid, and after its separation, the remainder of the liquid was repeatedly refractionated until the following fractions were obtained:

Fraction No.	Boiling Point (10 mm.), ° C.	Volume, Cc.	Per Cent by Volume.	$[\alpha]_D^{20}$.	d_{20}.	n_D^{20}.
I	104–114	Solid	....	−48.32°*	.....	.....
II	127–137	17.0	3.63	− 4.79°	0.9161	1.5112
III	137–147	19.0	4.16	− 1.78°	0.9231	1.5165

* In chloroform.

Lævo-Borneol.—The crystalline solid, after purification by recrystallization from alcohol, was found to melt at 203–203.5° C., corresponding favorably to the melting point of pure borneol.

For further identification, a phenylurethane, prepared in the usual manner and recrystallized from petroleum benzin, melted at 138° C. The melting point of the solid, in addition to that of the phenylurethane, was sufficient for the identification of borneol.

Lævo-Cadinene.—A portion of Fractions II and III was saturated with dry hydrochloric acid gas according to Wallach's method (7). The prepared chlorohydrate derivative was purified by recrystallization from a mixture of ether and alcohol. After drying, the crystals melted at 117–118° C. A bromohydrate derivative, prepared in a similar manner from each fraction, melted at 123–124° C.

The melting points of the above derivatives correspond to those of lævo-cadinene, which must be the chief component of these fractions.

Combined Acids: Acetic Acid.—After saponification of the high-boiling liquid, the alkaline washings were acidified with dilute sulfuric acid and extracted with ether. The residue amounted to 1.5437 Gm. and corresponded to 0.36 per cent of the original oil used for fractionation. The acid residue, entirely soluble in water, was neutralized with milk of lime, evaporated to dryness and extracted with alcohol. The material insoluble in alcohol was examined for acetic acid and identified by the usual qualitative tests. Acetic acid was undoubtedly the principal combined acid.

The residue soluble in alcohol was neutralized and precipitated with concentrated silver nitrate solution. The insoluble silver salt, after ignition, contained 51.40 per cent of silver. Silver isovalerate contains 51.65 per cent of silver. Since these results correspond so closely, it is possible that a small amount of isovaleric acid was present in the combined state.

SUMMARY.

The bark of *Abies grandis* yielded 0.37 per cent of volatile oil. The physical and chemical constants were determined in the usual manner. Traces of free acetic acid, phenols and aldehydes were present. The low-boiling liquid, representing 59.40 per cent of the oil, was composed of terpenes consisting chiefly of alpha-pinene, beta-pinene, beta-phellandrene and small amounts of camphene. The

high boiling liquid, representing 33.76 per cent of the oil, constituted mainly bornyl acetate and the sesquiterpene, lævo-cadinene.

Acetic acid was the principal combined acid with isovaleric acid possibly present in small quantities.

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THE PIGMENTS CONTAINED IN THE BARK OF THE ROOT OF CELASTRUS SCANDENS.*

BY O. GISVOLD.[1]

1. CELASTROL.

At one time some investigators thought that the chief pigment found in the outer bark of the root of *Celastrus scandens* was β-carotene. β-Carotene is of great importance because of its use as a standard for vitamin A, and therefore confirmation of its existence in a plant from which it might be easily isolated and purified was deemed advisable.

EXPERIMENTAL.

The material investigated was collected near Savage, Minn. The outer bark of the freshly collected roots of *Celastrus scandens* was readily removed with a vegetable grater. The bark thus obtained was ground and extracted with Skelly-solve B. The principal pigment contained in the bark was more soluble than other pigments present in lesser quantities, and therefore could be separated from them by fractional extraction. The first Skelly-solve B. extract contained so much pigment that it separated during the process of extraction. Upon prolonged extraction with fresh solvent, other pigments also separated. These varied in color from orange to yellow and some were even brown.

Celastrol.—Approximately 40 Gm. of the chief pigment were obtained as ruby-red cubes. They were recrystallized from a mixture of isopropyl ether and Skelly-solve B. The crystals melted apparently at 205° C. although there was evidence of decomposition. Additional recrystallizations failed to raise the observed melting point. Further investigations have shown that this compound contains hydroxyl groups and therefore the name celastrol is proposed. Celastrol is soluble in the fat solvents and in ethyl and methyl alcohols. It can be shaken from an ether solution with aqueous sodium hydroxide or sodium carbonate. The sodium salt forms a very dark red solution. The pigment cannot be shaken from ether by means of aqueous sodium bicarbonate. It forms a barium salt which is insoluble in methyl alcohol. Celastrol can be extracted from petroleum ether with 60 per cent or stronger aqueous methyl alcohol. The specific rotation of celastrol was very difficult to obtain because of the exceedingly dark-colored solutions.

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The original pigment as well as the derivatives made from it were dried at 100° C. over phosphorus pentoxide in a vacuum. The results of some of the analyses indicate that not all of the solvent was removed by this treatment.

Analysis—$[\alpha]_D^{25} = 0$ (in $CHCl_3$)

$C_{23}H_{36}O_3$	Calculated	C 76.69	H 10.00
	Found	C 76.66, 76.59	H 9.08, 8.65

Celastrol Acetate.—The acetate was prepared by heating celastrol with acetic anhydride and pyridine for one hour on a steam-bath. The acetate was yellow and melted approximately at 241° C.

Analysis—$[\alpha]_D^{25} = -54.2$ (in $CHCl_3$)

$C_{26}H_{34}O_5$	Calculated	C 73.00	H 8.00
	Found	C 73.27, 73.31	H 7.95, 8.30

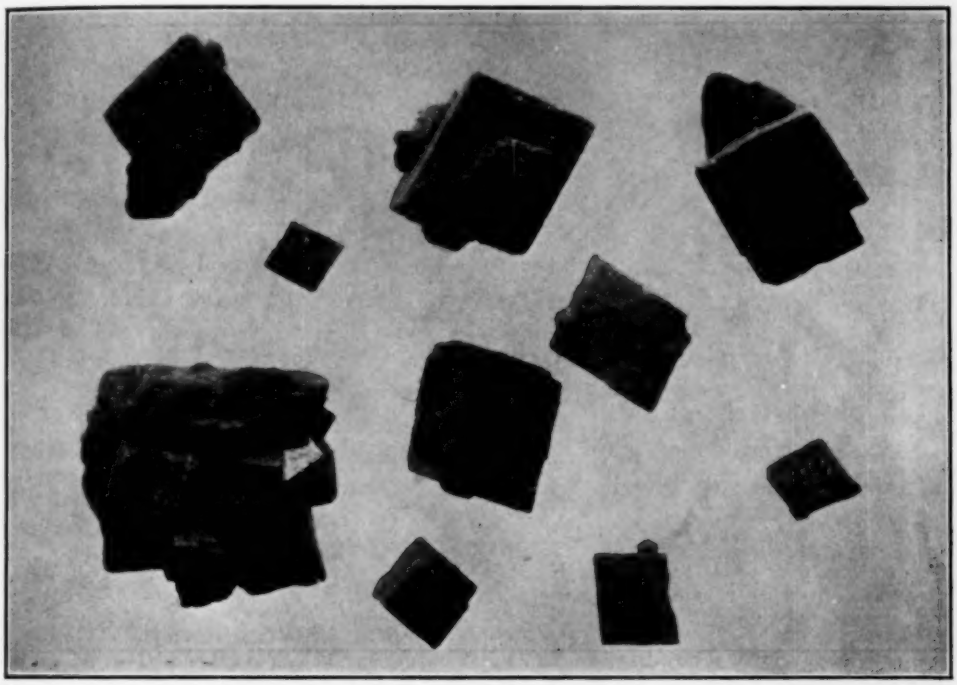

Fig. 1.—Celastrol.

Methyl Celastrol.—The methylated derivative was prepared by dissolving celastrol in dry ether and treating it with an excess of diazomethane. Methylation took place very rapidly. The derivative crystallized as orange needles from a mixture of ether and petroleum ether. M. p. 217.5–218° C.

Analysis—OCH_3

$C_{23}H_{32}O_3$	Calculated	8.71
	Found	9.19, 8.83; av. 9.01
	Molecular weight, rast 347	

Methyl Acetyl Celastrol.—The yellow acetate was methylated by means of diazomethane in dry ether. The yellow derivative was not obtained in crystalline form from a mixture of ether and Skelly-solve B. M. p. 132–133° C. After the compound was dried in a vacuum over phos-

phorus pentoxide, it gave the following methoxyl content, 8.99 and 9.27 per cent, respectively. These values appear to be higher than the theoretical. This may be due to traces of ether which could not be removed under the conditions of the experiment. However, the methoxyl content indicates that one methyl group was introduced into acetyl celastrol.

Acetyl Methyl Celastrol.—Methyl celastrol was acetylated with a mixture of acetic anhydride and pyridine. A yellow amorphous compound was obtained from a mixture of ether and Skelly-solve B. M. p. 132° C. The methoxyl content was 9.18 and 9.15 per cent, respectively.

Oxidation with Potassium Permanganate.—Five grams of celastrol were oxidized with cold aqueous alkaline permanganate according to the technique of Kuhn and Deutsch (1). Difficulty was encountered in attempting to obtain a crystalline oxidation fragment. The following technique overcame this difficulty. Purified sand was impregnated with the crude oxidation mixture and then extracted with Skelly-solve B. The Skelly-solve B. soluble fraction was crystallized only from dry ether. M. p. 252° C.

Reduction of Celastrol.—Celastrol was reduced in alcohol at 190° C. with Raney nickel as a catalyst.[1] One mole of hydrogen was absorbed by one mole of celastrol. A colorless solution

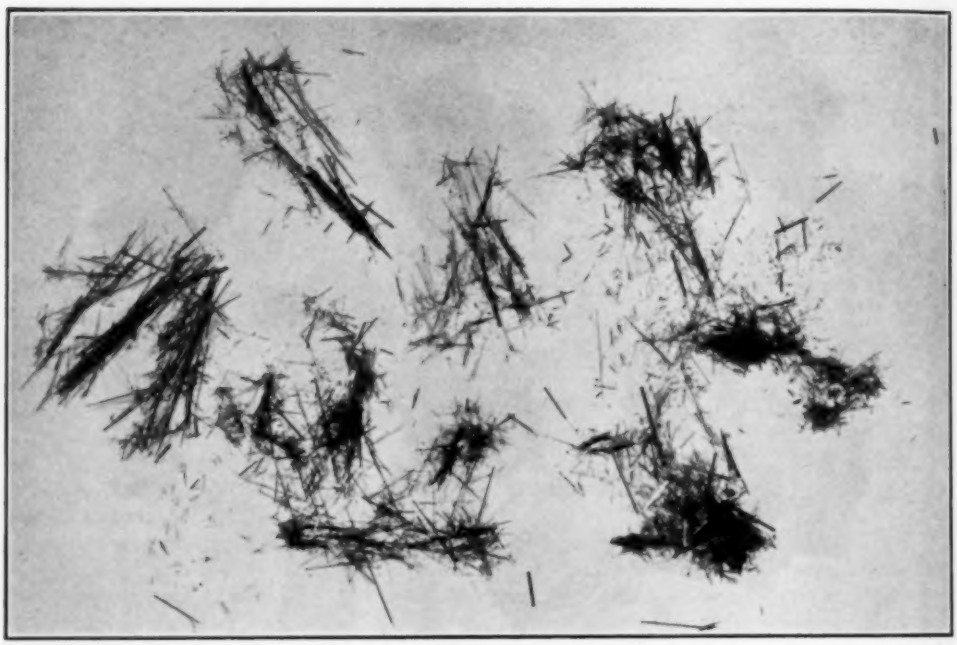

Fig. 2—Methyl Celastrol.

was obtained which soon became red upon standing in a beaker in the presence of the catalyst. An attempt to obtain a crystalline reduction product resulted in the recovery of ruby-red cubes. M. p. 203° C. When mixed with celastrol, no change in melting point was observed. The mother liquors yielded a very small amount of colorless needles (microscopic). These were not separated from the ruby-red cubes.

Iodine Number.—Wijs reagent (iodine and chlorine in glacial acetic acid) was used for the determination of the iodine number. The reagent was allowed to remain in contact with celastrol for twenty-four hours.

Analysis—$C_{29}H_{32}O_3$ with three double bonds.

Calculated	236
Found	233, 231, 230

[1] By Homer Adkins, University of Wisconsin.

Oxime.—An attempt to prepare an oxime according to the technique of Vavon and Anziani (2) failed.

Color Reactions.—Celastrol and methyl celastrol gave a green color with ferric chloride Acetyl celastrol, acetyl methyl and methyl acetyl celastrols gave no color with ferric chloride.

SUMMARY.

The bark of the root of *Celastrus scandens* contains no β-carotene. A red pigment has been isolated and named celastrol. Some of its physical properties and also those of some of its derivatives have been reported.

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NATURAL AND ARTIFICIAL CALAMINES FROM THE PHARMACEUTICAL, CHEMICAL AND PHARMACOLOGICAL STANDPOINTS.*,[1]

BY HELEN L. CREECH[2] AND C. O. LEE.[3]

INTRODUCTION.

The investigation of calamines began in 1803 when James Smithson (1) first distinguished chemically the differences between the silicate and the carbonate of zinc. Since then calamines have presented a challenging problem to pharmacists.

Prepared calamine N. F. VI is 98 per cent zinc oxide colored pink by the addition of a small amount of ferric oxide. It is extensively used for skin affections in the form of lotions and ointments. The question has been raised as to its merits over those of zinc oxide, and also whether the native calamine, generally described as impure zinc carbonate, and also precipitated zinc carbonate might not be better than the oxides.

This study was begun with the view of settling some of these questions.

HISTORY AND NOMENCLATURE.

There has been considerable confusion in the names applied to calamine. In the early history the oxide, carbonate and silicate of zinc were all known by the term cadmia or cadmea (4). At the present time, a native carbonate of zinc is called calamine by British mineralogists and smithsonite by Americans. The silicate of zinc is termed hemimorphite or electric calamine by the British, and calamine by the American mineralogists. In pharmacy, however, only the zinc carbonate has ever been recognized as calamine in both America and England.

The distinction between the silicate and carbonate of zinc by Smithson (1) in 1803 and the later work of Beudant (3) stimulated much interest in the commercial calamines. Following the work of Brett in 1837 many British and American workers turned to the analysis of them (6). The results in most cases showed that what appeared on the market as native zinc carbonate was barium sulfate colored with iron oxide. This situation was true in the British Isles, on the Con-

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[1] An abstract of a thesis presented to the faculty of Purdue University in partial fulfilment of the requirements for the Master of Science degree, August 1938.

[2] American Pharmaceutical Association Fellow, for the National Formulary Committee, 1937–1938.

[3] Professor of Pharmacy, Purdue University School of Pharmacy.

tinent and in America. Even as late as 1909 and 1910 reports indicate that barium sulfate was still often sold for calamine. About this time interest in the composition of calamines waned and effort was directed toward the improvement of the preparations of calamine and an increased knowledge of its mineralogy.

CALAMINE, ITS PREPARATION AND USE.

Natural calamine has been largely replaced by prepared calamine which is made by adding the proper amount of jeweler's rouge to a suspension of zinc oxide. When the color is evenly suspended, the water is evaporated, and the paste properly dried and reduced to a fine powder. A second method for making prepared calamine is to roast zinc carbonate with the proper amount of ferric chloride (10). Lotions and liniments of prepared calamine have come into vogue in the twentieth century.

The estimations of the therapeutic values of calamine have not changed greatly since the Roman period. It was then used in the treatment of ulcers and diseases of the eyes, being recognized as a drying and healing agent. For almost two thousand years the therapeutic virtues which Pliny and Dioscorides ascribed to calamine have been accepted.

To-day, although calamine is colored zinc oxide and not native zinc carbonate, it is still recognized as a soothing and protective agent in skin conditions such as eczema and sunburn. It is also used, to some extent, in ambulatory cases of ulcers as a protective agent for newly forming skin.

OFFICIAL PREPARATIONS.

The United States Pharmacopœias from 1820 to 1850 included monographs on the native carbonate of zinc. In the Pharmacopœia of 1850 precipitated zinc carbonate appeared for the first time. In the 1860 revision the precipitated zinc carbonate was retained and the native carbonate deleted. In the revisions from 1870 to 1910 the precipitated zinc carbonate was retained in the Pharmacopœia. It was, however, deleted from the 1920 revision.

The National Formulary IV included a monograph which made the native zinc carbonate and calcined zinc carbonate, with a small amount of ferric oxide, official permitting a choice. Thus the native zinc carbonate was official again after sixty years. The fifth edition of the National Formulary retained only the prepared calamine which was described as zinc oxide containing small amounts of ferric oxide and silica. The National Formulary VI has retained prepared calamine as zinc oxide, not less than 98% ZnO, with a small amount of ferric oxide.

EXPERIMENTAL.

The native calamine (smithsonite) used throughout this study was obtained from China through the courtesy of Dr. B. E. Read of the Lester Institute, Shanghai. The sample was received in the form of small lumps with loose powder adhering. It was flesh to salmon in color, appearing darker after being pulverized. It was found not to be radioactive. By means of a mortar and a pebble mill the lot was reduced to a powder and passed through a 200-mesh sieve. Throughout the experimental work it has been designated as Chinese calamine. The official prepared calamine has been studied along with the Chinese product.

CHEMISTRY OF CALAMINES.

Prepared Calamine N. F. VI and Chinese Calamine were subjected to qualitative and quantitative analysis. The results are given in Table I.

TABLE I.

	Analysis.	
	Qualitative.	Quantitative.
Prepared Calamine N. F. VI	Iron, zinc carbonate, oxide	Zinc oxide 98.87%*
Chinese Calamine (Smithsonite)	Iron, zinc, calcium, magnesium (trace) Aluminum, carbonate, oxide, insoluble residue (trace)	Zinc† 14.79% representing 18.43% zinc oxide

* The average of 2 assays.

† The average of 3 assays.

PRECIPITATED ZINC CARBONATE.

It was suggested that the antiseptic properties of precipitated zinc carbonate should be compared to those of calamine. It was prepared according to the directions of the U. S. P. V.

A semi-colloidal zinc carbonate was also prepared as follows: 100 ml. of 2.5 per cent sodium carbonate solution were added at the rate of 60 drops per minute to a solution of zinc sulfate, 6 Gm. in 200 ml. of a 2 per cent gelatin solution, with constant stirring. The precipitate was washed until free of sulfates. The particles assayed 1 to 1.5 microns in diameter.

BACTERIOLOGICAL TESTS.

A comparative study of the bacteriostatic property of the following compounds was made: prepared calamine N. F. VI, zinc oxide U. S. P. XI, zinc carbonate (A. R.), Chinese calamine, precipitated zinc carbonate and colloidal zinc carbonate. Each of these was incorporated in three different ointment bases and tested by the agar plate method using *Staphylococcus aureus* var. St. Louis and *Eberthella typhi* var. Rawlins as the test organisms.

Standard methods of testing were used and repeated sufficiently often to warrant reasonable conclusions as to results. No bacteriostatic action could be demonstrated for the six preparations named above. The variations in the bases employed had no effect on our results. The official ointment of ammoniated mercury was used as the control and gave uniformly positive results in every case.

A further attempt was made to test the bacteriostatic property prepared calamine N. F. VI, Chinese calamine, zinc oxide U. S. P. XI and zinc carbonate A. R. The agar cup plate method was used and *Eberthella typhi* var. Rawlins was the organism. A cup was made in the plate in the usual way and into it there was poured 1 Gm. of the powder suspended in water. The plates were incubated at 37° for 48 hours. The results were all negative.

It should be stated that this account is a brief summary of the results which are shown in several tables in the thesis. Inasmuch as the results are all negative, the tables are not being published.

A PROPOSED FORMULA FOR CALAMINE OINTMENT.

Objections have been made to the present official Ointment of Calamine, first because the directions for preparing it are not very specific and do not give a very smooth product. Second and perhaps more important, is the color. Because of the presence of yellow wax, lanolin and petrolatum the finished ointment has an unattractive color instead of an attractive pink which is obtained when white wax and white petrolatum are used. From a number of formulas which we have tried the following is suggested for consideration and study.

Prepared Calamine	17 Gm.
Liquid petrolatum or glycerin	11 Gm.
White wax	4 Gm.
Wool fat	4 Gm.
White petrolatum	64 Gm.

Procedure: Levigate the calamine with the liquid petrolatum or glycerin to a smooth paste. Melt the white wax, wool fat and the white petrolatum on a water-bath, remove and stir gently while cooling. Next add the cooled base, in divided portions, to the calamine and mix thoroughly to produce a smooth homogeneous ointment.

This ointment is easily prepared, has a good color, and spreads well when applied.

CLINICAL OBSERVATIONS.

The physicians of the Student Health Service, Purdue University, kindly coöperated in this study by using lotions of zinc oxide U. S. P. XI, prepared calamine N. F. VI, and Chinese calamine. The products were studied in part by being applied unilaterally to a symmetrical dermatitis. In some cases the lotions were applied and the results noted.

In all cases the patients reported that the applications were soothing. Such skin conditions as ringworm, drug dermatitis, dermatitis milia, soap dermatitis, dermatitis due to allergy and several unclassified cases of dermatitis were treated.

The physicians concluded that they could see no noticeable differences in the therapeutic action of these various lotions.

SUMMARY AND CONCLUSIONS.

1. Native American calamine is not available on the market. The samples which were obtained were silicates and not carbonate of zinc.

2. Several of the impurities which were reported as having been found in English calamine were also present in the Chinese calamine, namely, calcium, magnesium, iron and aluminum.

3. When tested in the form of ointments and suspensions by acceptable procedures, prepared calamine N. F. VI, zinc oxide U. S. P. XI, zinc carbonate A. R., Chinese calamine, precipitated zinc carbonate and semi-colloidal zinc carbonate were not bacteriostatic.

4. Clinical observations were made upon lotions of Chinese calamine, zinc oxide U. S. P. XI and prepared calamine N. F. VI and no differences as to their therapeutic action could be observed.

RECOMMENDATIONS.

1. In view of the fact that native American calamine is no longer available, and in view of the fact that native calamines, both foreign and domestic, are of uncertain composition and quality and furthermore that their superiority over prepared calamine as therapeutic agents has not been established, we recommend that prepared calamine be retained as an official product.

2. In view of the fact that the color of prepared calamine seems to have contributed to its acceptance as a medicinal agent, we recommend that the present formula for calamine ointment be changed so as to improve its color unless it can be shown that its therapeutic value is impaired by such a change.

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THE HOSPITAL DRUG BUYER.*

BY MORRIS DAUER.[1]

Those who have any conception of the task involved in regulating the purchase and distribution of drugs and medicines for use in a hospital, regardless of its size, realize the many angles and the various needs that must be catered to, whether they be general or specific.

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* Presented before the Sub-Section on Hospital Pharmacy, A. PH. A., Minneapolis meeting, 1938.

[1] Director, Department of Hospital Pharmacy, Brooklyn College of Pharmacy.

The pharmacist, like all who comprise the executive personnel of a hospital, is constantly reminded that his first obligation is to the patient whose needs must be unqualifiedly met and is given in the same breath a thousand and one restrictions with reference to expenditures for medical and pharmaceutical supplies. The medical staffs, particularly in a hospital, feel that they should not be hampered because the proper medicament cannot be immediately supplied but they insist on strict and rigid economies as far as budgeting pharmaceutical expenditures is concerned.

Practically speaking, this balance can only be realized when the medical and the pharmaceutical staffs get together from time to time and agree on certain official remedies which are used in rather large quantities and which can easily be manufactured in the hospital pharmacy at little cost.

However, there are many items which must be purchased, and try as much as you will, hospital pharmacists will definitely agree that the use of proprietary and trade-marked medicines and prescriptions is definitely on the uptrend and it is imperative that hospital administrators coöperate fully with these suggestions made by the author gained from practical experience so that the full measure of economic and clinical results may accrue to the hospital as an entity and to the patient as an individual.

It would be unsound to make a statement at this time that the hospital pharmacist can appear before his medical board and plead that they use only such drugs as appear in the official books in spite of the fact that many doctors even in this day and age insist that given a scalpel and three or four drugs they can practice all the medicine that there is.

The hospital pharmacist, on the other hand, must become more practical in this connection and ask the medical staff to coöperate upon a sound economic basis and simplify the use and purchase of such patent and proprietary medicines that have established merit, these purchases to be made exclusively from reputable pharmaceutical firms. This applies not only to patent and proprietary medicines but also to commonly used articles which cannot profitably be made in the hospital pharmacy.

Reputable pharmaceutical firms earn this distinction by their record of service to the medical and pharmaceutical professions and to the public. They restrict the operations of their sales force to the medical and pharmaceutical professions; their form of advertisement is conservative and educational and the results of clinical trial, both pro and con, are freely and honestly published.

In many cases after the indications for use have been fully described and set forth, the manufacturer feels free enough to warn the doctor of such cases where their product is counterindicated, thus reducing to a minimum the introduction of panaceas or cure-alls which the medical and pharmaceutical man knows is unscientific and which is unhesitatingly to be discouraged. These better firms, for the most part, conduct rather extensive research laboratories, wherein there are constantly developed new remedies to be used in the treatment of disease and they secure the services and coöperation of the best research medical scientists in their search for newer and more efficient therapeutic agents.

Well-known scientists too numerous to mention here are freely giving of their efforts to ailing mankind and to the promotion and elevation of the medical and

pharmaceutical professions through the medium of these pharmaceutical and technical laboratories. These firms are well known to all; they need not be mentioned by name and if their products be consistently ordered and used, the expenditures for specialty drugs will be kept at a constant and reasonable level in the hospital pharmacy.

It is common knowledge in our profession that as soon as a meritorious product makes its appearance many less qualified laboratories and manufacturing houses offer a substitute article which is represented to be just as good, identical in every respect, and which is quoted at one-half or one-third of the price of the original item.

Such unscrupulous and unprofessional competition should be discouraged because experience has shown that few substitutes are as reliable as the original product and, eventually, we will find our shelves cluttered up with countless duplicates.

The hospital pharmacist is frequently compelled to obtain these various duplicates at the insistence of members of the medical and surgical staffs and in spite of the fact that he sometimes misguidedly buys these articles in the name of economy, it can readily be seen that we are practicing a false economy that will prove more costly in the end.

If time and space permitted, I could show by actual reference the tremendous duplication that actually exists in numerous hospitals and institutions, and the irony of this situation is that many of these preparations are expensive such as hormone combinations, vitamin combinations, liver extracts and combinations, digitalis principles and the various combinations of biologicals.

It would not be amiss to make a plea at least to the better type of pharmaceutical manufacturers, even at a temporary commercial risk, not to duplicate every product introduced by a competitor.

Pharmacists in the retail field, not only in America but throughout the world, will support and sustain this plea.

This duplication is a large factor in the depletion of funds appropriated to the hospital pharmacist's budget; and his colleague in the retail field sadly admits that because of this deplorable condition most of his profts remain on the shelf.

Only too often is the question of price made the determining factor when purchasing pharmaceuticals and due consideration is not given to quality.

It is of paramount importance that quality and price be considered together; the prime essential, therefore, is to purchase at the best price from the most reliable manufacturer. Pharmaceutical firms who sell on the basis of price only should definitely be avoided.

Despite the fact that samples upon analysis come up to standard and meet specifications, unscrupulous manufacturers who compete mainly on price, contracts notwithstanding, will find some joker or loophole which safeguards their financial interests.

The economic factor in determining pharmaceutical expenditures must be based upon a sound, ethical foundation and hospital pharmacists must purchase pharmaceutical and medicinal products in a safe, sound and highly professional manner; by so doing they will secure for their institution preparations of the highest quality at reasonable prices from manufacturers of established and unquestionable integrity.

SUBSTITUTIONS, ITS EVILS AND NEED OF BETTER CONTROL.*

BY LYMAN F. KEBLER.[1]

The efficacy of medication depends in a very large measure upon the pharmacist's dispensing exactly what the doctor orders. Physicians come nearest the sick and are best qualified by education, training and experience, to decide what medication is best suited for their patients. Every honest pharmacist is opposed to the rascally business of substitution but still it goes on and on. Tampering with prescriptions is a serious proposition. In order to accomplish the greatest good for the suffering sick there must be complete harmony and coördination between the professions of Medicine and Pharmacy. It is sad to relate, but true, that substitution in Pharmacy has caused marked trouble down through the ages. I have met with plenty of it during the past forty years. I well recall, during the eighteen-nineties, the unpleasantness that resulted from the exposure and practical ruin of a prominent druggist in Philadelphia, for substituting in the filling of doctors' prescriptions. The leading instances of substitution and adulteration led to the all-inclusive drug definition in the National Food and Drug Law.

In the Report of the New York City Health Department, January 10, 1903, it is stated that 320 out of 373 samples of a drug purchased in drug stores were either gross substitutions or rank adulterations. These reported alleged adulterations were in truth largely just plain substitutions. The Food and Drug bills under active consideration by Congress, at the time, covered United States Pharmacopœial drugs only, a compromise satisfactory to but a few. Certain drug interests vigorously protested the limiting of drugs to be covered by a National law and requested a hearing on the subject, which was granted. At this hearing the glaring substitutions and adulterations reported by New York City Health Department and others were prominently featured. The drug representatives declared that the above limitations would preclude reaching thousands of substitutions and adulterations and would raise havoc with the filling of physician's prescriptions and the suffering sick. The hearing resulted in the following addition to the drug definition: "Also any substance intended to be used for the cure, mitigation and prevention of disease."

The amplified drug definition was included in a later Senate Food and Drug bill which caused a great rift in the various branches of the pharmaceutical profession. Strange as it may seem determined efforts were then made by the drug trade to prevent favorable action thereon by Congress, and Senator W. B. Heyburn, chairman of the Committee having charge of the bill, and other Senators were as determined to retain the enlarged definition. The bill failed to pass in the Senate, it was claimed largely because of the opposition to the amplification of the drug definition by the drug trade. Senator Heyburn was personally blamed for this failure, because he stubbornly and foolishly insisted on retaining the omnibus drug definition.

Senator Heyburn asserted that if the bill failed of passage he would introduce a like bill in the next, the 59th Congress. He made good his assertion. The bill

* Presented before the Section on Education and Legislation, A. PH. A., Minneapolis meeting, 1938.

[1] Former Chief of Drug Division, Bureau of Chemistry, U. S. Department of Agriculture.

contained the same offensive drug definition. Congressman Wm. P. Hepburn introduced a like bill in the House, without the inclusive drug definition. The contest was on and it was a bitter one. The bill passed the Senate with the enlarged drug definition, was finally accepted by the House and ultimately became a part of the National Food and Drugs Act, June 30, 1906.

A more extensive summary of this struggle, by the author, is contained in an article on "Physicians' Prescriptions" which will be published in a later issue of the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

Notwithstanding the fact that substitution played such a prominent part in the development and inclusion of the omnibus drug definition in the national law, the term substitution is not found in the act. It was possibly assumed that adulteration or misbranding, or both, covered substitution, but there are marked differences between substitution, adulteration and misbranding, as applied to drugs.

During the past year I came across an article on the old-time evil, written by O. U. Sisson, an eminent pharmacist, which both surprised and grieved me. It surprised me because of such an apparent prevalence of substitution in some places and grieved me because it reflects unfairly on some of my good apothecary friends in addition to giving the all-too-eager reporters the opportunity to speak reproachfully about the profession of Pharmacy. This occurred in a state which has had an anti-substitution law on its statute books for over thirty years. Said he, "So much has recently appeared in print regarding substitution in drug stores. Substitution literally means the giving of something of a lesser standard in place of the one prescribed or called for. No one having professional ethics at heart, can honestly condone or tolerate substitution in any form or nature in the dispensing of drugs, whether these be requested by physicians' prescriptions or otherwise."

He further calls attention to the fact that most of the alleged substitutions found during the Chicago hearings of the State Department of Registration and Education of the State of Illinois consisted in the dispensing of preparations of manufacturers other than the ones designated by the prescribing physicians. He does not consider this practice as objectionable as the substitution of a lower standard for the one called for. In the filling of prescriptions the only standard is the prescription. Substitution is substitution irrespective of any standard aside from the prescription itself. No one is justified in making any changes in any prescription without the advice and the consent of the physician. Otherwise the physician's objective may be thwarted. It is indeed morally if not legally wrong, and if the present laws or their enforcement do not reach the evil, the better element of the pharmaceutical profession should rectify the situation. If this is not done I venture the prediction that some outside agency will do the work for them. In fact, some of this has already been done and more can be expected in time.

In a private communication to me Druggist Sisson says, "This particular article was inspired because of the tirade carried on by the State Department of Registration and Education, in which many were accused. There were quite a few convictions and others were released for lack of evidence." Our friend makes the error, so frequently made by others, of criticizing or even reviling officers of the law, for doing their sworn duty in the enforcement of laws committed to their charge. It is a well-established axiom that laws will not enforce themselves and it is self-evident that enforcing any worth-while law will hurt some one.

State anti-adulteration laws made their appearance a century ago and later, but apparently no special efforts were made to enforce them, until those of the eighties were enacted. Those of us whose memories go back that far recall the abuse and calumny heaped on some of the state officials who enforced these laws as they saw them, without fear or favor. Those whose memories do not go back far enough can read with profit the records of the hectic activities in these fields. As to how well these laws have been enforced I have no definite knowledge, but it does seem that if they had been enforced in the spirit in which they were enacted there would be less substitution than seems to prevail at present.

Studies on the Qualities of Drugs in the District of Columbia and Court Decisions on Prescription Filling under the National Law.—Samples of standard drugs such as tincture of iodine, solution of citrate of magnesia, paregoric, soap liniment, elixir of iron, quinine and strychnine, tannic acid ointment, chloroform liniment, aromatic spirits of ammonia and others were purchased from time to time and tested as to purity and strength. The study was primarily made to ascertain the character of the medicines vended and possibly furnished on prescription. In cases where deviations from the standards were considerable, the vendors were either advised concerning the shortcomings or cited for hearings. The work was essentially educational. Some of the samples purchased later and found to vary unduly from the standards (2) were referred for court action. None of these cases was contested. A few of the cases passed on by the courts (3) and their defects are noted herewith; tincture of iodine, deficient in iodine and without potassium iodide; tincture of iodine, one-third standard strength in both iodine and potassium iodide; paregoric, one-third amount of opium required; soap liniment, methyl alcohol substituted in part for ethyl alcohol.

Complaints and criticisms were received at intervals about laxity and substitution in the filling of prescriptions. This was considered a part of the duties of the District Officials, but in time this line of work received some attention by the Bureau of Chemistry. The results (4) on the whole were fairly good, but in a few cases manifest carelessness existed and some substitution was disclosed. It was fully realized that this line of investigation reached into a new field and required the exercise of care. It was therefore decided to ascertain the cause or causes and, if possible, to help remedy the defects. No reasonable excuses were offered for the substitutions and, as noted above, the law does not specifically cover substitution. After weighing all of the evidence and the conditions obtaining, it was decided to take representative cases into Court. The Court passed on (5) and imposed modest fines in the following cases: substituting bismuth subcarbonate for bismuth subnitrate; antipyrin for acetphenetidin, and, in a third case, for short weights of two chemicals called for in the prescription.

There then appears to have been a period of quiescence in this line of work. At least neither of the indexes of the Notices of Judgments record any cases in the field of physicians' prescriptions. In November 1931 the Food and Drug Administration had about one hundred physicians' prescriptions filled by pharmacists in the District of Columbia. An examination of the products dispensed showed that some fifteen were sufficiently adulterated to cite the dispensers for prosecution. All but one of the druggists charged with violating the law entered pleas of guilty. The Court in some cases ordered that the imposition of a sentence be suspended, and each of the rest received a suspended sentence of twenty-five dollars. The case of the druggist who resisted the charge of adulteration had a decidedly different termination. After hearing the evidence the judge took the case under advisement and later in dismissing it ruled as follows: (6) "Inasmuch as the Government did not comply with the regulations made pursuant to the Act in regard to the procedure, it occurs to the Court that the same strict construction should apply to the Government as is contemplated against the defendant, and the case is accordingly dismissed." This is certainly a pretty severe indictment. The chief reason for this ruling was a failure to give the defendant a portion of the sample dispensed by the pharmacist.

Later, additional samples were collected on prescriptions by the Administration. Of these forty-two found their way into Court. It appears that the defendants tentatively agreed among themselves to abide by whatever decision might be rendered in any one case. The charge in the case tried was, briefly, that the compounded prescription fell below the professed standard under

which it was sold, because it should have contained 3 grs. of codeine sulfate, but in fact contained not less than 3.7 grs. of codeine sulfate. Indeed it actually fell above the standard instead of below it. The law does not specifically make it an offense to sell a drug above the professed standard. This charge therefore read something into the law that is not there, but the defendant could not very well raise this issue, because it involved a narcotic drug. On the whole it was not a very good case to try out an important issue. The case was actually tried out on demurrers. The Court sustained the demurrers, of which there were seven. The leading one in my opinion is the following: "That the Food and Drugs Act of June 30, 1906, does not apply to prescriptions compounded by a pharmacist" (7).

The above are certainly two vital decisions and if allowed to stand, the law to which they apply is practically inoperative, as far as concerns the dispensing of prescriptions, by pharmacists. Furthermore there seems to be little enthusiasm in either appealing the cases or bringing or prosecuting new cases. As things now stand there appears to be little specific legislation in the District controlling the filling of prescriptions, except in the case of certain narcotic drugs. It may be that something can be done under the District of Columbia Food and Drugs Act of 1898, but diligent search fails to disclose any action ever having been taken to deal with substitution in the case of physicians' prescriptions. A reading of the new Food, Drug and Cosmetic Act of June 25, 1938, does not seem to give any help on substitution problems.

According to the information communicated to me, all of the preparations covered by Notices of Judgments Nos. 26106 to 26116, inclusive, published in 1937, were purchased on physicians' prescriptions. A study of these documents fails to disclose that any of them were so purchased. This to my mind is omitting an important feature, particularly in view of the latter court decision, quoted above. The fact that they were purchased on physicians' prescriptons should be noted in the records published by direction of Congress. In the Notices of Judgment Nos. 5019, 5615 and 5622, published in 1918, dealing with the filling of physicians' prescriptions, this information is clearly set forth in the title of each case and is noted in the indexes. Any one desiring information on this point, in the later cases, will be compelled to look somewhere back of the published records, which in most instances is impractical.

In the above three Notices of Judgments, published in 1918, physicians' prescriptions are recognized as standards, in similar language of which the following is representative: "That its strength and purity fell below the professed standard and quality under which it was sold—." Similar language is contained in Notices of Judgments Nos. 26106 to 26116, inclusive, published in 1937, thus again recognizing physicians' prescriptions as standards. Prescriptions have from time immemorial been considered tacit standards, but these are the first instances in which they are definitely recognized as such in Government publications, issued by mandate of Congress.

Representative W. H. F. Lee was the first to use the term "misbranded" in Federal Food and Drug legislation. It appears several times in his comprehensive bill, introduced in Congress June 4, 1888. From this time on it retained a place in this type of bill and was finally made a part of the national law. Since then it has been utilized to meet various alleged violations, never intended originally. Modern dictionaries define the word "misbrand" briefly, to label or brand improperly or falsely. The definition in the law is much broader, but it is doubtful if much of it is applicable in cases of substitution in the filling of prescriptions, for the simple reason that aside from the parties immediately concerned, there is nothing on the label of the filled prescription excepting directions for its use.

There were two cases of substitution, Notices of Judgment Nos. 5019 and 5615, tried in the Court on the charge of misbranding. It must be admitted that this charge was far-fetched. There was no contest. These offenders had no standing in Court, but it is not good policy to bring action in a case of this character. It raises a question as to fairness of the enforcing officials. In the 1934 New York law, substitution and misbranding are defined in the same sentence. This may be helpful.

Anti-Substitution Laws in Some of the States and Territories.—There is definite evidence of record that substitution in the dispensing of prescriptions and otherwise is on a somewhat different footing than either adulteration or misbranding. Indeed there are some special laws on the subject, showing marked differences. Bulletin No. 98, revised, of the Bureau of Chemistry, 1908, contains some of the then-existing ones (8), namely: Arizona, Idaho, Illinois, Mary-

land, New York, Porto Rico and Tennessee. An effort will be made here to give brief extracts of these and other anti-substitution laws.

Controlling substitution in the filling of prescriptions in New York State, had its origin in 1864 (9), with a Commission appointed to codify the laws of the State. The Commission proposed the draft in pursuance of the frequent occurrence of accidents, even resulting in the loss of life, through mistakes in the putting up of prescriptions. Reference is made to a court case in which extract of belladonna was used in the filling of a prescription, in place of extract of dandelion, resulting in a dangerous illness. The proposed draft of the Commission was enacted into law in 1881 (10), and reads in part: "An apothecary, or druggist or any person employed as a clerk or salesman by an apothecary or druggist, who in making up any prescription or filling any order for drugs or medicines, willfully, negligently or ignorantly substitutes a different article than that prescribed or ordered, in consequence of which human life or health is endangered, is guilty of a misdemeanor." This phraseology certainly leaves ample opportunity for a clever substituter to substitute without fear of committing an offense. It should be noted that some of the laws enacted later on this subject contain a similar endangering proviso.

The same year, 1881, the New York State legislature enacted a so-called modern food and drug law (11) which shows that substitution and adulteration were even considered different evils and must be handled differently.

Both of these laws, materially amended, are retained to the present time. The anti-substitution act as amended in 1907 (12) forbids any person putting up a drug, medicine, food or preparation, or substituting or dispensing a different article from that prescribed or ordered, or in any way deviating from the terms of the prescription. He is at liberty, except in the case of prescriptions, to recommend the purchase of another article than the one called for or ordered, but it must be of a similar nature, with the full knowledge of the purchaser.

A conviction under this law is punishable as a misdemeanor. For a second conviction the offender must be sentenced to imprisonment for a term of not less than ten days nor more than one year, and to the payment of a fine of not less than ten dollars nor more than five hundred dollars. For a third conviction he is not only liable for the above penalties but "shall forfeit any right which he may possess under the laws of this State at the time of such connection to engage in any capacity in the compounding, preparing or dispensing medical prescriptions or orders for drugs, medicines or foods or preparations used in the medical practice." This drastic act, so different from the early one of 1881, is at present in force and should certainly curb substitution, if even moderately well enforced.

Fifty years ago, 1887, while Idaho was still a territory, its legislative body passed a law (13), prohibiting the substitution of a different article for any article prescribed or ordered or otherwise deviating from the terms of the prescription or order, declaring such to be a misdemeanor, in case human life or health is endangered, or a felony if death ensues. These contingencies look serious but in fact provide loopholes for chronic substituters. The same law was enacted (14) in Arizona in 1901 and for Porto Rico in 1902 (15). The penalties in this law in a measure resemble those in the 1881 New York Law.

The State of Maine passed an excellent short law in 1899 (16) covering substitution in the filling of physicians' written prescriptions. It reads as follows: "Whoever, engaged in the business of an apothecary, knowingly uses any drugs or ingredients in preparing or compounding a written prescription of any physician different from those named in the prescription, shall upon conviction be fined not less than five nor more than one hundred dollars." This law commends itself for its brevity, simplicity, definiteness and fairness to all concerned. Such a law, if fairly enforced, is bound to minimize and possibly eradicate the malicious practice of substitution, in time.

In 1901 the legislature of Tennessee made it unlawful (17) to substitute any drug or medicine for the one mentioned in the physician's prescription, or aiding or abetting in committing the offense. The fine on conviction is not less than twenty-five dollars nor more than one hundred dollars for each and every conviction.

Under the 1901 drug adulteration law (18) of Illinois, any person who substitutes or causes to be substituted, without notification to the purchaser, one material for another, shall be liable to prosecution under this act and if convicted shall be liable for all of the expenses incurred by the Board of Pharmacy, and in addition, for the first offense, shall be liable to a fine of not less

than fifty dollars nor more than one hundred dollars. Fines for each subsequent offense are not less than seventy-five dollars nor more than one hundred and fifty dollars.

In 1907 the law was amended (19) to include substitution in the filling of prescriptions This law is still in effect. The idea of the dispenser notifying the purchaser in case of substitution in the filling of prescriptions is rather unique and one is prompted to inquire as to its practicability. The enforcement of this act was lodged (20) with the Department of Registration and Education in 1917.

The anti-substitution law of Maryland, passed (21) in 1902, forbids knowingly selling or delivering of any medicine or drug to any person, other than that called for or ordered by such person, or using any drug or medicine other than that called for in a physician's prescription. A violation is adjudged a misdemeanor and a conviction thereof is punishable by a fine of not less than one hundred dollars nor more than five hundred dollars, or correspondingly severe imprisonments, or both such fines and imprisonments and in addition any person so convicted forfeits "the right to practice Pharmacy under any certificate or registration issued under the laws of this State." This is one of the early, if not the earliest, drastic anti-substitution laws.

North Carolina enacted an anti-substitution law (22) in 1937, along the lines of the Maryland act. A violation is adjudged a misdemeanor and on conviction thereof is punishable as such. The law contains an interesting proviso. It reads: "This Act shall apply to registered drug stores and their employees only." What the purpose of this restriction is, few are able to make out.

A review of the above summary of the state anti-substitution laws calls to mind the unsatisfactory conditions that prevailed in the states in the matter of food and drug adulteration, prior to the enactment of the national law. It is believed that some action should be taken to bring about uniform state anti-substitution laws and methods for their enforcement. It is therefore suggested that the chairman of this section appoint a committee of three, to study the subject during the coming year and make a report at the next annual meeting of the association.

REFERENCES.

(1) Sisson, O. U., *Chicago Retail Druggists' Assoc. News*, 49, 22 (July 1, 1937).

(2) Kebler, Lyman F., JOUR. A. PH. A., 2, 514, and *J. Ind. Eng. Chem.*, 5, 484 (1913); Kebler, Lyman F., and associates, JOUR. A. PH. A., 6, 614 and 684 (1917).

(3) Notices of Judgments Nos. 2424 and 2425, respectively, U. S. Department of Agriculture (1913); Notices of Judgments Nos. 5041 and 5043, respectively, U. S. Department of Agriculture (1918).

(4) Kebler, Lyman F., and associates, JOUR. A. PH. A., 6, 687 (1917).

(5) Notices of Judgments Nos. 5019, 5615 and 5622, respectively, U. S. Department of Agriculture (1918).

(6) Notice of Judgment No. 26108, U. S. Department of Agriculture (1937).

(7) Justice W. J. Casey, District of Columbia, Police Court Rec. (April 12, 1937).

(8) Kebler, Lyman F., Bureau of Chemistry, Bull. No. 98, revised, entitled, "Drug Legislation in the United States (1909)."

(9) Penal Code Draft, by Commission, page 166 (1864).

(10) Laws, Penal Code 3, 100 (1881).

(11) *Ibid.*, page 553 (1881).

(12) *Ibid.*, page 1500 (1907).

(13) Idaho, Rev. Stat., page 744 (1887).

(14) Arizona, Rev. Stat., page 1246 (1901).

(15) Porto Rico, Rev. Stat., and Codes (Penal Code), page 552 (1902).

(16) Maine Public Laws, page 107 (1899).

(17) Tennessee Acts, Chap. 27, page 41 (1901).

(18) Illinois Laws, page 238 (1901).

(19) *Ibid.*, 382 (1907).

(20) Illinois Civil Administration Code, 3, 7 (1917).

(21) Maryland Laws, page 148 (1902).

(22) North Carolina Public Laws, Chap. 59, page 103 (1937).

ASSOCIATION BUSINESS

AD INTERIM BUSINESS OF THE COUNCIL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 1938–1939.

Office of the Secretary, 2215 Constitution Ave., Washington, D. C.

LETTER NO. 8.

June 14, 1939.

To the Members of the Council:

62. The Connecticut College of Pharmacy Student Branch. Motion No. 20 (Council Letter No. 7, page 326) has been carried with the following members voting in the affirmative: YES, Ke, Hi, Sw, La, Li, Ck, Dm, Ga, Co, Mi, Ro, Je, Fi, Ch, Mo.

63. Motion No. 21 (Council Letter No. 7, page 326) has been carried with the following members voting in the affirmative: Ke, Hi, Sw, La, Li, Ck, Dm, Ga, Co, Mi, Ro, Je, Fi, Ch, Mo.

64. Motion No. 17 (Council Letter No. 6, page 250) has been carried with the following members voting in the affirmative: YES, Ke, Hi, Sw, La, Li, Ck, Dm, Ga, Co, Mi, Ro, Je, Fi, Ch.

65. The Kilmer Prize. In the Report of the Committee on Requirements for the Ebert and Kilmer Prizes (JOUR. A. PH. A., page 818, item (*d*), Sept. 1938) which was approved, it was recommended that the Kilmer Prize "be made to consist of a suitable gold key, and that the difference between the cost of the key and the annual income from the bequest be awarded to the winner in cash to assist him in attending the annual meeting of the ASSOCIATION to receive the award."

Later, Dr. H. W. Youngken, chairman of the Committee on Kilmer Prize, submitted sketches for the key and recommended that the L. G. Balfour Company, Attleboro, Mass., be invited to submit finished designs and prices. This Company advised that the sketches with minor modifications are satisfactory and a suitable photograph of the late Dr. Kilmer has been located, through the coöperation of Dr. Fischelis, from which the profile model for the key can be prepared.

The L. G. Balfour Company quote a price of $35 for the first key, which includes the cost of modeling, $25; and $10 for each key thereafter.

The income of the Kilmer Fund for 1938 amounted to $82.50 and it is planned to deduct $10 for the medal and the expenses of Committee on Kilmer Prize, covering postage, etc., from this amount and present the remainder to the winner of the prize.

The $25 for the modeling will be paid for out of accumulated income.

(*Motion No. 22*) It is moved by Kelly that L. G. Balfour Company be authorized to prepare the Kilmer Prize key with the understanding that the necessary modeling will cost $25 and that each key will cost $10.

A vote is called for on this motion but it will be considered as tentative if there is objection or if additional information is desired.

66. Use of Text of N. F. VI. The following communication has been received from Chairman DuMez of the Committee on Publications:

"I have looked over the manuscript for the new edition of Backmann and Bliss' book on Physiology and it is being returned herewith. Blackiston had permission to use a portion of the text of the N. F. in the 3rd edition of this book and I can see no reason why permission should not be granted again.

"I, therefore, recommend that permission be granted Blackiston to quote portions of the text of the N. F. VI in the new edition of Backmann and Bliss' 'Essentials of Physiology and Pharmacodynamics' on the same terms as previously made."

(*Motion No. 23*) It is moved by DuMez that P. Blackiston Son & Co., Inc. be granted permission to use portions of the text of N. F. VI in the Third Edition of Backmann & Bliss' "Essentials of Physiology and Pharmacodynamics" with the usual fee of $5.00 and with the customary acknowledgment.

67. Applicants for Membership. The following applications, properly endorsed, accompanied with the first year's dues, and recommended by two members of the ASSOCIATION, have been received:

Nos.: 567, George T. Nowicki, 4704 E. 104th St., Cleveland, O.; 568, Theodora A. J. Leckband, 1505 W. North Ave., Chicago, Ill.; 569, Marius K. Sorensen, 318 Missouri Ave., Alliance, Nebr.; 570, Sister Mary Grace Kujawa, 2649 N. Hamlin Ave., Chicago, Ill.; 571, John P. Ruddick, 1705 M St., N. W., Washington, D. C.; 572, John Dee McPherson, Hamilton Drug Store, Colfax, Wash.; 573, A. E. Hanham, 43 Victoria St., Toronto, Can.; 574, Lawrence L. Wheeler, 508 King St., Wenatchee, Wash.; 575, Ernest L. Beals, 234 N. 29th St., Corvallis, Ore.; 576, Albert A. Padula, 3006 Burnside Ave., St. Joseph, Mo.; 577, Henry W. Heine, 815 N. Grant St., W. Lafayette, Ind.; 578, C. J. Zufall, 617 Waldron St., W. Lafayette, Ind.; 579, Samuel L. Ross, 144 Clinton St., Toronto, Can.; 580, Archibald J. Jewell, 2346–54 Sedgley Ave., Philadelphia, Pa.; 581, Leland N. Brown, 6816 Market St., Upper Darby, Pa.; 582, Lewis J. Kleckner, Admiral Apts., Philadelphia, Pa.; 583, William H. Hughes, 1510 W. Allegheny Ave., Philadelphia, Pa.; 584, Maurice L. Augenblick, 5632 Beaumont Ave., Philadelphia, Pa.; 585, Harry L. Richards, Ypsilanti State Hospital, Ypsilanti, Mich.; 586, Jack Gordon, 810 Oliver Ave., N., Minneapolis, Minn.; 587, George Grider, 118 W. Oak, Louisville, Ky.; 588, John J. Furlong, 711 S. 33rd St., Louisville, Ky.; 589, William M. Spahn, 2510 W. Oak, Louisville, Ky.; 590, Malcolm J. MacLeod, 40 Spruce St., Watertown, Mass.; 591, Charles A. McCarthy, 162 Castle St., Geneva, N. Y.; 592, Josef Legner, Jr., 411 Virginia Ave., La Porte, Ind.; 593, Abraham J. Fleisher, 2400 N. 19th St., Philadelphia, Pa.; 594, Harry Kaye, 1536 Grand Concourse, Bronx, N. Y.; 595, Myrle Engstrom, 4732 Oxford Ave., Phila., Pa.; 596, Norman A. Wack, 118 E. Lancaster Ave., Wayne, Pa.; 597, John P. Barlement, 2449 Kensington Ave., Phila., Pa.; 598, George N. Beaulieu, Jr., Manuel Ave., Johnston, R. I.; 599, Robert M. Besancon, 808 S. Wood St., Chicago, Ill.; 600, Morton J. Schnaper, 3405 Fessenden St., N. W., Washington, D. C.; 601, Lillian Passen, 547 S. Fulton Ave., Baltimore, Md.; 602, Ernest J. Cater, R. F. D. No. 2, Mosinee, Wis.; 603, Edgar E. Alexander, Tuskegee Institute, Ala.; 604, Frederick F. Grimmer, 1226 St. Claire St., Green Bay, Wis.; 605, D. W. Leary, Biltmore Pharmacy, Biltmore Hotel, Atlanta, Ga.; 606, Eleanor J. Banister, 2101 John Ave., Superior, Wis.; 607, Odin Thorstenson, 514 Olive Way, Seattle, Wash.; 608, Albert G. Worton, 803 Bancroft St., Indianapolis, Ind.; 609, Joseph B. Wade, 1068 Virginia Ave., Indianapolis, Ind.; 610, Julius W. Hollmann, Box 205, Shiner, Tex.; 611, Vernon F. Beyer, Box 216, Elizabeth, N. J.; 612, Lee H. Macdonald, 608 N. Kalamazoo St., Paw Paw, Mich.; 613, Howell R. Jordan, 125½ W. 7th, Austin, Tex.; 614, Mrs. Sara W. Carmody, 3415 Boulevard, Jersey City, N. J.; 615, Herbert Skoglund, 4838 Haddon Ave., Chicago, Ill.; 616, Lewis Smith, 3315 Junius St., Dallas, Tex.; 617, Albert H. Gelman, 1743 N. W. 31st Ave., Portland, Ore.; 618, Jacob P. Lee, c/o Lees Drug Store, Meuomonic, Wis.; 619, William Radoff, 782 Lexington Ave., New York City; 620, Emil C. Fanto, McKesson & Robbins, Inc., Box 548, Bridgeport, Conn.; 621, Charles R. Shalz, 1053 E. Woodland Ave., Chico, Calif.; 622, William C. Hickey, 314 S. Main St., Fall River, Mass.; 623, Sister Mary Paul Johnston, St. Thomas Hospital, Akron, O.; 624, Newton H. Vogel, 29–28—163 St., Flushing, L. I., N. Y.

(*Motion No. 24*) Vote on applications for membership in the ASSOCIATION.

68. Refunding Loan on Lot No. 7. In Council Letter No. 19, 1935–1936, item 123 (JOUR. A. PH. A., page 467, May 1936) Dr. Dunning recommended that Treasurer Holton and Secretary Kelly be authorized to borrow $36,400 from the Maryland Trust Company, on a mortgage note for 3 years at 4% interest payable quarterly, to pay the mortage note for the same amount at 5½%, payable semi-annually, held by the George Washington University in payment for Lot No. 7. The recommendation was approved (see Council Letter No. 21, 1935–1936, item 131, JOUR. A. PH. A., page 471, May 1936) and the loan completed on May 1, 1936. When the note matured, and after conferring with the Committee on Finance, the secretary took up the question of a renewal with the Maryland Trust Company and arrangements have been made to extend the loan for a further period of three years at 3% interest, payable quarterly, which represents a considerable saving. The charges will amount to about $15. The extension agreement is as follows:

Washington, D. C.

June 6th, 1939.

The loan of $36,400 made by the Maryland Trust Company to the AMERICAN PHARMACEUTICAL ASSOCIATION under date of May 1st, 1936, secured on property in the City of Washington, District of Columbia, to wit, certain lots in Square 62 (being premises situated on Constitution

Avenue between Twenty-second and Twenty-third Streets), which became due and payable on May 1st, 1939, with interest at the rate of 4% per annum, payable quarterly, is hereby extended for a further period of three years, with interest at the rate of 3% per annum, instead of 4% per annum, until paid, payable quarterly.

All other provisions of the Deed of Trust dated May 1st, 1936, made by the AMERICAN PHARMACEUTICAL ASSOCIATION to D. Luke Hopkins and Carlyle Barton, Trustees, securing the loan, are to remain unchanged and in full force.

AMERICAN PHARMACEUTICAL ASSOCIATION.

By_____
President,
Owner of equity in property.

ATTEST:

_____
Secretary.

ATTEST:

Maryland Trust Company.

James B. Bird,
Secretary

By D. Luke Hopkins,
Vice-President,
Holder of loan.

(*Motion No. 25*) It is moved by Swain that the extension agreement as quoted be approved, that President Lascoff and Secretary Kelly be authorized to sign the agreement and that S. L. Hilton be authorized to sign the new note for $36,400 as attorney in fact for the ASSOCIATION.

69. Joint Meeting Executive Committee of the N. A. R. D. and Council of A. Ph. A. In accordance with the usual arrangement, this joint meeting will be held during the Atlanta meeting of the A. PH. A. Secretary Dargavel of the N. A. R. D. has accepted an invitation for the joint meeting on Wednesday, August 23rd, in Room E, Hotel Atlanta Biltmore, at 2:30 P.M. A meeting of the Council has been scheduled at that time and can be continued after the program of the Joint Meeting is completed.

E. F. KELLY, *Secretary.*

LETTER NO. 9.

June 24, 1939.

To the Members of the Council:

70. Use of Text of N. F. VI. Prentice Hall, Inc., New York, N. Y. issue, in addition to other services, a Food, Drug and Cosmetic Service, in loose-leaf form, in which is furnished information to those interested in this legislation and its enforcement, and have requested the privilege to quote the titles of the drugs official in the N. F. VI.

Chairman DuMez of the Committee on Publications writes as follows: "In response to your letter of the 14th inst., it is recommended that Prentice Hall, Inc., be granted the privilege of including a list of drugs official in the N. F. VI in their loose-leaf service and that the usual fee be charged for the same.

(*Motion No. 26*) It is moved by DuMez that Prentice Hall, Inc. be granted permission to quote the titles of the drugs official in the N. F. VI in their loose-leaf service, with the usual fee of $5.00 and the customary acknowledgment.

71. Tentative Program of the Atlanta Meeting. Local Secretary Wilson with the approval of the Local Committee and the Committee on Standard Program, submits the tentative program as attached to this letter. The management of the Hotel Atlanta Biltmore has approved the assignment of meeting rooms and the program so far as it affects the A. A. C. P. and the N. A. B. P. have been approved by the secretaries of both organizations.

The major changes in the program are: that the meeting of the National Conference on Pharmaceutical Research has been changed from the Saturday preceding the meeting until

Tuesday afternoon, August 22nd; and that since the Local Committee did not require Thursday afternoon for an entertainment feature, several meetings have been scheduled for that period thus relieving the congestion on Wednesday and Friday afternoons. Otherwise, the program in general follows the usual arrangement.

(*Motion No. 27*) It is moved by Kelly that the tentative general program of the Atlanta meeting be approved as submitted.

72. Applicants for Membership. The following applications, properly endorsed, accompanied with the first year's dues, and recommended by two members of the ASSOCIATION, have been received:

Nos. 625, Muriel E. Miller, Salem Hospital, Salem, Mass.; 626, Samuel L. Antonow, Chicago Beach Hotel, Chicago, Ill.; 627, Chester M. Cobb, 489 Bullocks Point Ave., Riverside, R. I.; 628, Badros H. Ohannessian, 96 Laurel St., Watertown, Mass.; 629, Mother Edward Von Simonovic, 3400 Esplanade Ave., New Orleans, La.; 630, Brendan Dixon, 1879 Calif. Ave., Long Beach, Calif.; 631, Hugh Clinton Gardner, Jr., 359 S. Maine St., Baldwin Park, Calif.; 632, William T. McCarten, 33 Dundonald St., Toronto, Can.; 633, Vincent M. Harrington, Marianna, Ark.; 634, Mary Hosmer, 75 W. Center St., Midvale, Utah.

(*Motion No. 28*) Vote on applications for membership in the ASSOCIATION.

E. F. KELLY, *Secretary.*

THE CLEVELAND SOCIETY OF HOSPITAL PHARMACISTS.

The newly founded Cleveland Society of Hospital Pharmacists has just completed a most successful year. The society was founded just slightly over a year ago, when a group of hospital pharmacists from our city met to determine how they might arrange a get-together in order to discuss hospital pharmacy problems. A constitution was drawn up and it was agreed that membership was to include only hospital pharmacists. We were to have eight meetings a year. These meetings were to be held at the various hospitals and at the School of Pharmacy of Western Reserve University.

The meetings throughout the year proved to be most educational and valuable to us. Such subjects as, "The Manufacture of Sterile Solutions;" "Pro and Con of Buying Sterile Solutions;" "Kline Test for Syphilis;" "Treatment of Pneumonia;" "Functions of a Pharmacy Committee;" "Narcotic Control Within an Institution;" "United States Public Health Service and the Relationship to the Pharmacist;" and "Anode Rubber and Its Use in the Hospital," were presented at the meetings. Dr. D. S. Kline, Mt. Sinai Hospital; Dr. C. Garvin, City Hospital; and Mr. Robert Porter, Akron City Hospital, were among the speakers. One evening the members were guests of The Goodyear Rubber Co. and had a very interesting trip through the plant.

Our society was instrumental in the founding of the new Ohio Society of Hospital Pharmacists, which was formed last April during the Ohio Hospital Association Convention at Columbus. Two of our members were made officers of this state society.

. . . . . .

Our last meeting was held on May 31, 1939. This was our annual dinner meeting and the election of officers took place. The new officers of the Cleveland Society of Hospital Pharmacists are: *President*, Robert Stockhaus, City Hospital; *Vice-President*, John Miller, Huron Road Hospital; *Treasurer*, G. Brown, U. S. Marine Hospital; *Secretary*, Robert Kumpf, City Hospital; *Corresponding Secretary*, Gertrude Horsch, University Hospital.

It has been planned that we are to have many interesting meetings this fall and it is our hope that every hospital pharmacist within this territory will become a member. We would like to have hospital pharmacists from Canton, Akron, Youngstown, Elyria, Lorain and other nearby cities, for we feel that the future of hospital pharmacy will depend upon the united efforts of every hospital pharmacist. It is possible that a National Hospital Pharmacists Association will be formed in the very near future.

ROBERT A. KUMPF, *Secretary.*

CORRECTION.

In the June issue of the JOURNAL, 1939, end of first paragraph, page 339, the reference should read JOUR. A. PH. A., for November 1934, page 1137.

PROCEEDINGS OF THE LOCAL AND STUDENT BRANCHES

CHICAGO.—The April meeting was held Tuesday evening, the 18th, in the College of Medicine Buildings. The newly elected officers were introduced to those in attendance by Secretary R. E. Terry.

The main address was delivered by Mr. Jack Levant of McKesson, Fuller, Morrisson, Inc., on "Problems of Mutual Interest to Manufacturer, Service Wholesaler and Retailer." The main problem of the above three groups, as given by Mr. Levant, is the placing of merchandise in the hands of the consumer with profit to all. The service wholesaler occupies a central position among these, acting to see that the manufacturer is accorded proper distribution of his products and that the retailer has on his shelves those products which the consumer demands.

Itemizing the responsibilities of the service wholesaler to the manufacturer, the following were among those mentioned by Mr. Levant: (1) The wholesaler offers the most economical and the best distribution service; (2) The wholesaler acts as a stabilizing influence for the manufacturer as an envoy of goodwill, and in maintaining the latter's fair trade policies; (3) The wholesaler takes care of advertising in many cases and sees to the proper placement of manufacturer's goods, thus aiding in elimination of waste caused by improper placement and unwise distribution.

Considering the relationship to the retailer, Mr. Levant brought forth the following points: (1) The wholesaler gives the retailer the product when he wants it; (2) The wholesaler gives credit to the retailer helping maintain the latter's business in many cases under stressing circumstances; (3) The wholesaler is prepared to furnish financial advice to the retailer at any or all times; (4) The wholesaler holds valuable dealers' meetings of educational nature to proprietors, clerks, etc.

Mr. Levant also brought forth the point that, in many cases, if the retailer was more "selling conscious" and less "buying conscious" profitable business would show a definite increase.

Mr. Levant invited discussion from the floor into which several members entered with enthusiasm showing that the problems discussed by him were of vital interest to those present at the meeting.

EDWARD E. VICHER, *Secretary.*

MICHIGAN.—The May meeting was held in Ann Arbor, on the 16th, in conjunction with the Pharmaceutical Conference sponsored by the University of Michigan, College of Pharmacy. The Conference was opened by Dr. Howard B. Lewis, director of the College of Pharmacy, and chairman of the Conference. The address of welcome was made by Prof. C. H. Stocking, who gave a brief history of the Conference and invited the pharmacists of Michigan to make use of the many facilities of the University.

Dr. Lewis then introduced Dr. W. F. Rudd, dean of the School of Pharmacy, Medical College of Virginia. Dr. Rudd spoke on "Some Present Pharmaceutical Problems, Socialized Pharmacy and Working Conditions in Retail Pharmacy." Dr. Rudd stated that the deans and professors of the Colleges of Pharmacy will have to exert effort to bring into Pharmacy men of high educational standing. He urged pharmacists to bring about changed conditions, which they alone can do. A discussion followed, led by Dr. Nathan Sinai of the University of Michigan, who agreed with Dr. Rudd and said Pharmacy must take the lead in bringing about demand for pharmaceutical care. Dr. Sinai was followed by Mr. Lee H. MacDonald of Paw Paw, who also agreed.

Mr. John H. Webster, past-president of a number of pharmaceutical associations, defended the pharmacist of to-day. The average pharmacist is independent and not dependent upon the various agencies for relief as is the case with many professions in these trying times. He said Pharmacy is an American institution and is meeting the demands of the public in rendering the service required by the community. The corner drug store is ever ready for any emergency that may arise, thereby protecting public health.

The following addresses were enjoyed: "The Introduction and Developments of Antiseptics," Dr. F. F. Blicke; and "Methods of Evaluation of Antiseptics," Dr. M. H. Soule, both of which were illustrated. The Conference then adjourned and an inspection tour made of the H. H. Rackham School of Graduate Studies.

At the business meeting in the evening, reading of the minutes was dispensed with. The Nominating Committee made a report, and the following were elected for the ensuing year:

President, H. A. K. Whitney; *First Vice-President*, John Karagulis; *Second Vice-President*, Charles Schenck; *Secretary*, Bernard A. Bialk, *Treasurer*, Fred F. Ingram; and *Chairman of the Program Committee*, Dean R. T. Lakey.

The meeting then adjourned to the Amphitheatre of the H. H. Rackham School where Dr. Carl V. Weller, University of Michigan Medical School spoke on, "The Pathology of Syphilis as a Public Health Problem," illustrating his talk with slides. The address was most interesting and instructive.

A rising vote of thinks to the speakers and the faculty of the College of Pharmacy, University of Michigan, was then in order, after which the session adjourned, with all the members eager to return for the Ninth Pharmaceutical Conference next May.

BERNARD A. BIALK, *Secretary.*

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE.

SUBSECTION ON PHARMACY.

The two sessions of the subsection held during the Milwaukee meeting, June 20th, were devoted to a symposium on the vitamins with particular reference to their standardization.

Dr. Aaron Arnold in his report on thiamin pointed out that interfering substances limit the value of the chemical methods of determination and that the biological method based on growth is the most reliable procedure. Simpler and more rapid methods for the determination of thiamin and new criteria of its functions will make it possible to determine whether the level for optimum nutrition is appreciably above the requirement level.

Dr. P. H. Phillips in comparing the methods for the assay of riboflavin based on fluorescence, color and photolysis and growth promotion, pointed out that the bio-assay method is the most accurate method now known but that the colorimetric method offers much promise when applied to the degradation products of this vitamin. Methods using micro-organisms are economical, rapid and accurate for the determination of trace levels. Evidence has been obtained which indicates that riboflavin may be necessary for the deaminization of amino acids and the formation of urea in the liver. It plays an important rôle in nerve nutrition in chicks which exhibit neuromalacia on low riboflavin diets and recover rapidly when the deficiency is supplied by the administration of riboflavin.

Dr. C. A. Elvehjen reviewed the procedures which led to the isolation of the nicotinic acid fraction of the *Vitamin B complex*. He showed that while chemical procedures, bacterial growth methods and bio-assays offer possibilities, the most reliable assay procedure at present is the curative method applied to dogs in which black tongue has been induced by feeding a suitable nicotinic acid deficient basal ration. It was emphasized that a chemical method of assay is greatly needed so that our knowledge of the distribution of nicotinic acid as well as other factors in foods may be made known. When this knowledge is available, it will be possible to modify the diet, particularly in areas where pellagra is prevalent and fortify the diet with nicotinic acid if necessary to prevent the disease.

Dr. D. W. Wooley discussed the chick antidermatitis factor and pantothenic acid of the *Vitamin B complex*. The assay of the former is best carried out on chicks by noting the growth and prevention of dermatitis as compared to chicks on a basal diet. A method for the determination of pantothenic acid which is rapid, economical and accurate has been devised. It is based on the discovery that pantothenic acid is essential for the growth of a wide variety of hemolytic streptococci. An assay by this method can be completed in twenty-four hours and it excels the animal method in precision. All of the authors of papers pertaining to the *Vitamin B complex* emphasized the need for chemical methods of assay and for methods of assay which would permit the determination of the concentration of vitamins in the blood.

Dr. A. Black critically examined the factors which influence the accuracy of vitamin A assays. He stated that the biological methods measure the combined vitamin A activity of the various compounds which may become available as vitamin A to the rat and that the method is not specific for any particular kind of vitamin A. Methods based on the measurement of the absorption of light by means of spectrophotometers have been widely used and are the most accurate and give the most information about the sample.

Vitamin E, the anti-sterility vitamin, was reviewed as to its sources, isolation, chemistry, physiological activity and assay by Mrs. Flemintine P. Dann. The production of pure alpha tocopherol (Vitamin E) offers promise of leading to a more quantitative method than the present bio-assay.

GLENN L. JENKINS, *Chairman of the Program Committee.*

PERSONAL AND NEWS ITEMS.

Mr. Frank L. McCartney, of Norwich, N. Y., presented the Museum, American Institute of Pharmacy, with three old drug jars of decorated porcelain. These belonged to a set of five and it is hoped that the other two jars may be obtained for the ASSOCIATION. The decorations consist of gold, with trailing rosebuds.

Georgia Pharmaceutical Association met on June 20th to 22nd, in Savannah. Among the speakers were: J. J. McManus, chief of Atlanta Station of U. S. Food and Drug Administration, "The Pharmacist and the Food, Drug and Cosmetic Law;" Richard M. Charlton, city editor, *Savannah Morning News;* Dr. W. H. Myers, president, Georgia Medical Association, "Trend of Medicines;" and L. N. Camp, "U. S. P. and N. F. Propaganda." The meeting was a great success.

Mississippi Pharmaceutical Association met June 19th to 21st, at Meridian. The attendance was good, program interesting and entertainment delightful. Among the speakers were: Hon. Thomas L. Bailey, member of the State Legislature who was instrumental in securing passage of the Mississippi Fair Trade Bill; George L. Sugg, "Better Business;" and Dr. J. P. Wall, president, Mississippi State Medical Association.

The American Dental Association held its convention in Milwaukee, Wis., July 17th to 21st. This, the 81st annual meeting, marked another milestone in scientific achievement, professional prestige and general good fellowship and offered Pharmacy in Wisconsin a splendid opportunity to coöperate with Dentistry.

The Pennsylvania Pharmaceutical Association met in Johnstown, June 19th to 22nd. There was open discussion on: "The Vanishing Ten Per cent;" "Odd Price Figures in Drug Products;" "Elimination of Fictitious Prices;" "Honest Prices on New Products;" "Combination Deals." Among the speakers were: Dr. John J. Shaw, Secretary of Health, Commonwealth of Pennsylvania; Dr. R. P. Fischelis, "Coherence in Pharmaceutical Thought;" Joseph F. McDonnell, Jr., chief chemist, Pennsylvania State Board of Pharmacy; Michael McFadden, Director Narcotic Control, Department of Health, "Experiences in Narcotic Enforcement."

Endo Products, Inc., New York City, have recently purchased a modern concrete and steel structure, at Richmond Hill, L. I. After alterations have been completed the new structure will house all administrative and technical departments of the organization. A sales office will be maintained at the present address.

Plans at the new building call for the construction of new modern laboratories housing adequate facilities for production and research involved in pharmaceutical manufacturing. Greatly enlarged research facilities will be made available where work can be continued along the lines of development of natural and synthetic hormone and vitamin substances, the primary object being to develop these active materials for parenteral administration.

When the transfer to new quarters has been completed, all technical personnel will be augmented when necessary with highly specialized chemists, physicists and pharmacists, etc. The technical staff is headed by Dr. Roland A. Bosee, Director of Laboratories, and Dr. S. M. Gordon, Director of Research.

The Louisville College of Pharmacy held Commencement Exercises on June 6th, in the Scottish Rite Temple. Twenty-six received the degree of Bachelor of Science in Pharmacy.

Mr. Turner F. Currens, New York City, donated to the Museum of the AMERICAN PHARMACEUTICAL ASSOCIATION, on June 18, 1939, four mortars and pestles, which he collected during his travels in Sweden (1), Brittany (2), French Morrocco (3) and Holland (4). This is a valuable addition to our ever-growing collection.

We are advised that the Texas Senate passed the state Fair Trade bill on June 15th. The bill had previously been passed by the House. It is believed that the Governor will sign the bill and thus make Texas the 45th state to have passed this legislation. This victory marks a continuous advance against the proponents of unfair trade tactics.

On June 5th ground was broken for the Bunting-Foxwell Library, Washington College, Chestertown, Md., which is being built by funds largely contributed by **Dr. George A. Bunting,** president of Noxzema Chemical Co., Baltimore, Md. Dr. Bunting is an alumnus of Washington College.

Glenn Slocum, son of Mr. J. W. Slocum, Indianola, Iowa, received his Ph.D. degree from the University of Maryland on June 3rd. He has been assigned to work for the Government in Denver, Long Beach, Calif., and New Orleans.

At the Commencement of the Philadelphia College of Pharmacy and Science, on June 7th, the following men received honorary degrees: **C. Mahlon Kline,** president of Smith Kline and French, Inc., Doctor of Science; **Dr. Solomon Solis-Cohen,** Philadelphia physician, Doctor of Science; **Henry V. DeHaven,** retail pharmacist, Master of Pharmacy; and **Charles T. Pickett,** pharmacist, Master of Pharmacy.

A member of one of our Student Branches writes, "The JOURNAL has proven to be a wonderful thing for my work and I do not want to miss out on any copy."

The School of Pharmacy, University of Maryland, announces the establishment of three research fellowships by the William R. Warner Company, a pharmaceutical house of New York City. The post-graduate fellowships have been awarded to **Mr. George P. Hager, Jr.,** who last year enrolled in the Graduate School of Colorado University, and to **Kenneth E. Hamlin, Jr.,** of the Graduate School of the University of Maryland; the post-doctorate fellowship is awarded to **Dr. Melvin F. W. Dunker,** who received his Ph.D. from Maryland on June 3, 1939. The three Fellows will do their work in pharmaceutical chemistry.

Dr. Marvin R. Thompson of the Warner Institute for Therapeutic Research sailed July 3rd on the Nieuw Amsterdam with his wife and two daughters to visit the European branches of William R. Warner and Co., Inc., and to assist in the establishment of a new research laboratory in Berlin.

The American Pharmaceutical Manufacturers Association held its thirty-second meeting at Skytop, Pa., June 25th to 29th. The meeting was the largest in attendance that the Association has ever had. Mr. F. A. Lawson, of the E. L. Patch Co., was elected as *President* and Mr. S. Barksdale Penick, Jr., of S. B. Penick & Co., as *Secretary*. Place of meeting for 1940 will be voted on by mail.

The Bureau of Professional Licensing, Department of Public Instruction, Harrisburg, Pa., issued a report of the State Pharmacy Laboratory for its first year of operation, 1938. As the laboratory tests drugs submitted to it by investigators of the Bureau of Professional Licensing, a total of 867 samples were tested and the report gives a very interesting summary of the results.

Dr. S. L. Hilton, Washington, D. C., presented the Library of the AMERICAN PHARMACEUTICAL ASSOCIATION with a bound volume of the JOURNAL A. PH. A., for the year 1912. This is a very timely gift as we are having requests for these old volumes and they are becoming exhausted.

William R. Warner & Co., Inc., New York City, announce the establishment of the following Research Fellowships under the Warner Institute for Therapeutic Research, for the year beginning July 1, 1939:

At Columbia University, College of Physicians and Surgeons; under Prof. James W. Jobling, Department of Pathology; a post-doctorate fellowship to **Henry S. Simms, Ph.D.,** for the continuation of his work on Arteriosclerosis.

At the University of Maryland, School of Pharmacy; under Prof. Walter H. Hartung, Department of Pharmaceutical Chemistry. (See preceding column.)

At the Warner Institute for Therapeutic Research; under Dr. Marvin R. Thompson, director; a post-doctorate fellowship to **P. P. Zapponi, Ph.D.,** for studies in Physical Chemistry.

OBITUARY.

GEORGE T. KERMOTT.

Mr. Kermott passed away at his home, Duluth, Minn., on June 2nd, just a few weeks before the Minnesota Pharmaceutical Association was to open its convention; and since he was president, it was necessary to appoint some one to take charge of the meeting.

Mr. Kermott graduated from the College of Pharmacy of the University of Minnesota, was associated with a prominent pharmaceutical house for some time, and also several stores in the state, prior to purchasing the Clinic Pharmacy in Duluth. He was a member of the Minnesota State Board of Pharmacy for many years and was a member of the AMERICAN PHARMACEUTICAL ASSOCIATION.

A Masonic funeral was held on June 5th. Surviving are his widow and one daughter, Elizabeth.

MRS. CHARLES H. LAWALL.

On June 25th, Mrs. Millicent Renshaw LaWall, wife of the late Dr. Charles H. LaWall, passed away at her summer residence, Longport, N. J. Funeral services on the 29th, at 2:00 P.M., from the Funeral Home of Andrew J. Bair & Son, were private.

Mrs. LaWall was a graduate of the Philadelphia College of Pharmacy and Science and had been a member of the AMERICAN PHARMACEUTICAL ASSOCIATION since 1911. Among some of her activities were: Assisting Chairman Joseph P. Remington in the revision of the U. S. Pharmacopœia VIII, secretary of the Civic Club of Philadelphia on Foods and Home Economics, and also served as vice-chairman, and was director for a number of years of the Pharmaceutical Laboratory, Women's Medical College of Pennsylvania.

In recent years Mrs. LaWall assisted Dr. LaWall in his work, and on her own account and as co-author with him, she presented a number of historical articles on pharmacists of early periods, among them one on "Charles Marshall of Philadelphia" and "Apothecary Shops of Colonial Days," and rendered contributory search in connection with "Four Thousand Years of Pharmacy," by Charles H. LaWall, and assisted him in other research.

HOWARD J. SIEGFRIED.

H. J. Siegfried, prominent pharmacist of Frankford, Philadelphia, Pa., and trustee of the Philadelphia College of Pharmacy, died Tuesday, the 27th, at Somers Point, N. J., aged seventy years.

Mr. Siegfried graduated from the Philadelphia College of Pharmacy in 1893, and five years later established his business from which he retired in 1929. He was a director of the Philadelphia Wholesale Drug Co., a member of Frankford Presbyterian Church, the Masonic order and numerous druggists' organizations throughout the state.

Mrs. Annie Clewell Siegfried, his widow, and two daughters, Dorothy and Mrs. J. Franklin Styer, survive; also a brother, Robert L. Siegfried, of Nazareth, Pa. Funeral services were held on Saturday with interment in Bethlehem, Pa.

BOOK NOTICES AND REVIEWS.

Die Fermente und ihre Wirkungen, by PROF. DR. CARL OPPENHEIMER, supplement, Lieferung 10, four illustrations, 1938. Publishers, Dr. W. Junk; verlag The Hague. Price, N. florins 10.

The author is an outstanding authority on ferments; the 10th consignment includes under B., the nature and properties of ferments. The author asks that co-workers send him research and reprints dealing with ferments and to include older work back to the year 1925, but certainly present reports. He desires to have continued articles and states that he has opportunity to place copies with publications and requests that reprints be sent promptly after appearance. The work will soon be completed and as all workers are interested, the author hopes for prompt response to his requests; communications should be addressed to him Berlin W. 15, Kurfüerstendamm 61.

Enzymologia. Editor Carl Oppenheimer and the collaborators are from all sections of the world, well and favorably known in the science of chemical ferments and the publication is outstanding in the science. The publisher is Dr. W. Junk, the Hague. Subscription price for the volume of about 400 pages, illustrated, Dutch florins 15.

A few of many contributors are named: Dr. Dean Burk, Wilmington, Del.; S. L. Edlbacher, Basel; R. Ege, Copenhagen; H. Jorgensen, Copenhagen; Sir O. G. Hopkins, Cambridge; L. Michaels, New York; W. H. Peterson, Madison, Wis.; J. B. Sumner, Ithaca; C. Voegtlin, Washington; J. J. Willaman, Bristol, Pa.; C. V. Smythe, New York; W. R. Ringer, Utrecht.

Those engaged in this field of work find this publication helpful.

Pharmaceutical Therapeutics, by ELDIN V. LYNN. Second Edition. 430 pages. Published by McGraw-Hill Book Co., New York City. Price, $4.00.

Vitamin B_1 (Thiamin) and Its Use in Medicine, by R. R. WILLIAMS, Bell Telephone Laboratories, New York City; and T. D. SPIES, Associate Professor of Medicine, University of Cincinnati. 411 pages, with frontispiece. Published by Macmillan Co., New York City. Price, $5.00.

PROGRAM OF THE 87th ANNUAL MEETING AMERICAN PHARMACEUTICAL ASSOCIATION AND AFFILIATED ORGANIZATIONS, HOTEL BILTMORE, ATLANTA, GA. AUGUST 20th TO 26th, 1939.

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General Information.

The Arrangements Committee for the 1939 A. PH. A. Convention sincerely hopes that you will have a most profitable and enjoyable time during your stay with us. Please feel free to call on any member of the Committee if they can be of service to you in any way.

ROBERT C. WILSON,
Local Secretary.

Register Promptly.—The Registration Desk is located in the Lobby. Be sure to receive the official badge and tickets covering the entertainment features—examine and carry them with you—exchange the coupons promptly as requested.

The Information Desk.—Inquire here for Garage and Automobile Service; Lost and Found Bureau; Physician, Dentist, Pharmacist, Nurse or Hospital, etc.

Bulletin Board.—Telephone Calls, Telegrams and Announcements will be posted near Registration Desk.

Join the AMERICAN PHARMACEUTICAL ASSOCIATION—Application Blanks at the Information Desk.

Time.—All meetings and events are to be held on Central Standard time. Set your watch by the Hotel Clock.

THE GENERAL PROGRAM.

August 14th–18th, 1939.

Plant Science Seminar, Blue Ridge College, Blue Ridge, N. C.

Sunday, August 20th.

9:30 A.M.	Council, A. PH. A., Room E.
2:00 P.M.	Council, A. PH. A., Room E.
2:00 P.M.	Committee on Pharmaceutical Syllabus, Room G.
2:00 P.M.	Joint Meeting, Executive Committees of A. A. C. P. and N. A. B. P., Room A.
8:00 P.M.	Opening Concert. Negro Choir in Garden of Hotel.

Monday, August 21st.

9:00 A.M.	American Association Colleges of Pharmacy, Executive Committee, Room A.
9:30 A.M.	Conference of Teachers of Chemistry, Room F.
	Conference of Teachers of Pharmacy, Room C.
	Conference of Teachers of Pharmacognosy and Pharmacology, Room B.
	Conference of Teachers of Pharmaceutical Economics, Room G.
9:30 A.M.	National Association Boards of Pharmacy, Ballroom.
12:30 P.M.	Luncheon, N. A. B. P.
1:30 P.M.	N. A. B. P., Ballroom.
1:30 P.M.	A. A. C. P., First Session, Pompeian Room.
6:30 P.M.	Joint Dinner—N. A. B. P. and A. A. C. P., Ballroom.
8:00 P.M.	A. A. C. P., Second Session, Pompeian Room.
8:30 P.M.	Conf. Pharm. Law Enforcement Officials, First Session, Room F.

Tuesday, August 22nd.

9:30 A.M.	Joint Conference, A. PH. A., N. A. B. P. and A. A. C. P., Ballroom.
12:15 P.M.	Luncheon, Committee on Recipe Book.
2:00 P.M.	N. A. B. P., Ballroom.

2:00 P.M. A. A. C. P., Third Session, Pompeian Room.
2:00 P.M. National Conf. on Pharmaceutical Research, Room G.
6:30 P.M. Dinner, Rho Chi Society, followed by Annual Meeting.
6:30 P.M. Dinner, National Conf. on Pharm. Research.
8:30 P.M. First General Session, A. PH. A., Ballroom.

Wednesday, August 23rd.

8:00 A.M. Breakfast, Members U. S. P. Committee of Revision and Board of Trustees.
9:30 A.M. First Session, House of Delegates, Ballroom.
10:30 A.M. Meeting of the Women's Auxiliary, Pompeian Room.
12:45 P.M. Luncheon, Kappa Psi Fraternity and Lambda Kappa Sigma Sorority.
12:45 P.M. Luncheon, Phi Delta Chi Fraternity.
2:30 P.M. Joint Session, Council A. PH. A. with Exec. Com. N. A. R. D., Room E.
2:30 P.M. First Session, Scientific Section, Ballroom.
2:30 P.M. First Session, Section on Education and Legislation, Pompeian Room.
2:30 P.M. First Session, Section on Practical Pharmacy and Dispensing, Room F.
2:30 P.M. First Session, Section on Historical Pharmacy, Room A.
2:30 P.M. First Session, Section on Pharmaceutical Economics, Room G.
2:30 P.M. First Session, Conf. Pharm. Assn. Secretaries, Room B.
3:30 P.M. First Session, Sub-Section on Chemistry, Room D.
3:30 P.M. Meeting, Committee on Nominations, Room 127.
3:30 P.M. Meeting, Committee on Resolutions, Room 129.
7:30 P.M. Joint Banquet, A. PH. A. and Related Organizations, Piedmont Driving Club (leave Hotel at 6:00 P.M.).

Thursday, August 24th.

9:30 A.M. Second General Session, A. PH. A., Ballroom.
12:30 P.M. Veteran Druggists Luncheon.
2:30 P.M. First Session, Sub-Section on Hospital Pharmacy, Room C.
2:30 P.M. Conf. of State Committees on U. S. P.-N. F. Promotion, Room A.
2:30 P.M. Conference of Professional Pharmacists, Room G.
2:30 P.M. Second Session, Conf. of Law Enforcement Officials, Room F.
6:00 P.M. Georgia Barbecue on the Grounds of the Biltmore Hotel.
8:30 P.M. Second Session, House of Delegates, Ballroom.

Friday, August 25th.

9:30 A.M. Joint Session, Scientific Section and Section on Practical Pharmacy and Dispensing, Ballroom.
9:30 A.M. Second Session, Section on Education and Legislation, Pompeian Room.
10:30 A.M. Second Session, Sub-Section on Hospital Pharmacy, Room C.
10:30 A.M. Second Session, Scientific Section, Ballroom.
12:30 P.M. Luncheon, Hospital Pharmacists.
2:30 P.M. Third Session, Scientific Section, Ballroom.
2:30 P.M. Second Session, Section on Practical Pharmacy and Dispensing, Room F.
2:30 P.M. Second Session, Section on Historical Pharmacy, Room A.
2:30 P.M. Second Session, Section on Pharmaceutical Economics, Room G.
2:30 P.M. Second Session, Conf. Pharm. Assn. Secretaries, Room B.
6:30 P.M. Dinner, Former Presidents, A. PH. A., Room C.
7:30 P.M. Meeting, Committee on Resolutions, Room B.
8:00 P.M. Final Session House of Delegates, Pompeian Room.
10:30 P.M. Cotton Ball, Ballroom.

Saturday, August 26th.

9:30 A.M. Final General Session, A. PH. A., Ballroom.
1:00 P.M. Council, A. PH. A., Room E.

THE GENERAL SESSIONS.

ASSOCIATION OFFICERS.

President, J. Leon Lascoff; *Honorary President*, W. C. Anderson; *First Vice-President*, A. O. Mickelsen; *Second Vice-President*, George A. Moulton; *Secretary*, E. F. Kelly; *Treasurer*, C. W. Holton; *Editor of the Year Book*, A. G. DuMez.

OFFICERS-ELECT, 1939–1940.

President, A. G. DuMez; *First Vice-President*, F. O. Taylor; *Second Vice-President*, F. J. Cermak; *Members of the Council* (for three years), H. C. Christensen; R. P. Fischelis; Ernest Little.

First General Session, Tuesday, August 22nd, 8:30 P.M., Ballroom.

1. Call to Order.
2. Reading of Communications.
3. Messages of Welcome: Bonnie Brown, President Georgia Pharmaceutical Association; M. J. Long, President Atlanta Retail Druggists Association; A. Clifford Ayers, President Fifth District Pharmaceutical Association.
4. Report of the House of Delegates. Charles H. Rogers, Chairman.
5. Address of the President, J. Leon Lascoff.
6. Introduction of the President-Elect, A. G. DuMez.

7. Address by Hon. E. D. Rivers, Governor of Georgia, "Public Health."
8. Unfinished Business.
9. New Business.

Second General Session, Thursday, August 24th, 9:30 A.M., Ballroom.

A Brief Memorial Session will be held.

1. Minutes of the First General Session.
2. Reading of Communications.
3. Report of the House of Delegates on the President's Address and on Other Matters, Charles H. Rogers, Chairman.
4. Address by Malcolm T. MacEachern, Associate Director, American College of Surgeons.
5. "The Place of Pharmacy in Health Insurance in London, England," Herbert M. Skinner, Royal Northern Hospital, London.
6. Report of the Committee on Maintenance, H. A. B. Dunning, Chairman.
7. "The United States Pharmacopœia," E. Fullerton Cook, Chairman, Committee of Revision.
8. Unfinished Business.
9. New Business.

Third General Session, Saturday, August 26th, 9:30 A.M., Ballroom.

1. Minutes of the Second Session.
2. Reading of Communications.
3. Final Report of the House of Delegates, Charles H. Rogers.
4. Unfinished Business.
5. Award of the Ebert Prize.
6. Award of the Kilmer Prize.
7. Installation of Officers.
8. Address of the President, A. G. DuMez.
9. Final Adjournment.

THE COUNCIL.

Chairman, S. L. Hilton; *Vice-Chairman*, Glenn L. Jenkins; *Secretary*, E. F. Kelly; R. P. Fischelis, Ernest Little, R. L. Swain, H. C. Christensen, H. A. B. Dunning, P. H. Costello, Roy B. Cook, J. Leon Lascoff, E. N. Gathercoal, A. O. Mickelsen, Geo. A. Moulton, C. W. Holton, A. G. DuMez, C. H. Rogers.

Sessions—Room E.

Sunday, August 20th, 9:30 A.M. and 2:00 P.M.; Wednesday, August 23rd, 2.30 P.M.; Saturday, August 26th, 1:00 P.M.

THE HOUSE OF DELEGATES.

Chairman, Charles H. Rogers; *Vice-Chairman*, R. A. Kuever; *Secretary*, E. F. Kelly.

First Session, Wednesday, August 23rd, 9:30 A.M., Ballroom.

1. Call to Order.
2. Roll Call of Delegates.
3. Reception of Fraternal Delegates.
4. Opening Remarks by Chairman Charles H. Rogers.
5. Appointment of Committee on Nominations and on Resolutions.
6. Annual Report of the Council.
7. Annual Report of the Treasurer, C. W. Holton.
8. Annual Report of the Secretary, E. F. Kelly.
9. Executive Session Devoted to a Discussion of Food, Drug and Cosmetics Legislation and Other Topics.
10. Receipt of Resolutions, Reports and Other Communications—all of which must be in writing.
11. New Business.

Second Session, Thursday, August 24th, 8:30 P.M., Ballroom.

1. Roll Call of Delegates.
2. Minutes of the First Session.
3. Receipt of Reports and Other Communications from the ASSOCIATION, the Council and the Sections.
4. Receipt of Reports, Resolutions and Other Communications—all of which must be in writing.
5. Executive Session for the Consideration of Matters of Vital Importance to Pharmacy in America.
6. Reports of Committees on Social and Economic Relations, R. P. Fischelis; on the Modernization of Pharmacy Laws, R. L. Swain; on Local and Student Branches, Ernest Little; on Pharmacy Week, John E. O'Brien; on Weights and Measures, M. N. Ford; on Legislation, E. F. Kelly; on Pharmacists in the Government Service, H. Evert Kendig; on Prescription Tolerances, ————; on the Council on Pharmaceutical Practice, E. Fullerton Cook; on Dental Pharmacy, G. C. Schicks.
7. Election of the Honorary President, Secretary and Treasurer of the ASSOCIATION on Nomination by the Council.
8. Report of the Committee on Nominations.
9. Report of the Committee on Place of Meeting, W. F. Rudd.
10. Report of the Committee on Resolutions.
11. New Business.

Third Session, Friday, August 25th, 8:00 P.M., Pompeian Room.

1. Roll Call of Delegates.
2. Minutes of the Second Session.
3. Receipt of Reports and Other Communications from the ASSOCIATION, the Council and the Sections.
4. Reports of Committees: on Professional Relations, L. A. Seltzer; on Membership, E. F. Kelly; on U. S. Pharmacopœia, E. H. Wirth; on Horticultural Nomenclature, H. W. Youngken; on Physiological Testing, J. C. Munch; on Wm. Procter, Jr., Memorial Fund, J. E. Hancock; on Endowment Fund, ————; to Study Courses in the History of Pharmacy, C. O. Lee; on Press Relations, R. W. Rodman.

5. Final Report of the Committee on Resolutions.
6. Unfinished Business.
7. Installation of Chairman and Vice-Chairman.
8. Final Adjournment.

THE SECTIONS.

Please Note—Order of Business and Order of Programs are subject to change and additional numbers by Sections, if found expedient to do so.

Papers of the Sections are numbered at the request of the Local Committee to assist in an effort to flash titles of papers being read in different Sections at the same time—See the Official Program. The flash designations are as follows: Scientific Section, "Sc.;" Education and Legislation, "E.;" Practical Pharmacy, "Ph.;" Hospital Pharmacy, "Hosp.;" Pharmaceutical Economics, "PEc.;" Historical Pharmacy, "Hi.;" Papers of Joint Sessions of Sections are not given—See Official Program.

SCIENTIFIC SECTION.

(Flash "Sc.")

Chairman, C. F. Lanwermeyer; *First Vice-Chairman*, J. B. Burt; *Second Vice-Chairman*, F. J. Goodrich; *Secretary*, F. E. Bibbins; *Delegate to the House of Delegates*, B. V. Christensen.

First Session, Wednesday, August 23rd, 2:30 P.M., Ballroom.

Chairman's Address—C. F. Lanwermeyer.
Secretary's Report—F. E. Bibbins.
Committee Reports:
Board of Review of Papers, F. E. Bibbins, Chairman.
Committee on Monographs, E. E. Swanson, Chairman.
Special Committees.
Appointment of Nominating Committee.
General Business.

PAPERS.

1. "The Approximate Phytochemical Analysis of Athyrium Felix-Foemina," Malcolm S. Trupp and Forest J. Goodrich.
2. "Rapid Staining Methods in Plant Histology," Robert S. McLean.
3. "The Pharmacognosy of the Parathyroid," Heber W. Youngken. (Lantern.)
4. "Phyto-Chemical Study of Copernicia Cerifera Martius," R. A. Bowers and A. H. Uhl.
5. "Toxicity of Selenium-Cystine," Alvin L. Moxon.
6. "Potentilla Anserina," A. Richard Bliss, Jr., and Collaborators.
7. "The Histology of Salvia Officinalis," Elbert Voss and Frank Fortunate. (Lantern.)
8. "Mirabilis Jalapa, A Substitute for Jalap," Heber W. Youngken. (Lantern.)
9. "A Comparative Study of the Menthols," A. Richard Bliss, Jr., and H. Bryson Glass.
10. "A Pharmacological Study of the Active Principle of Passiflora Incarnata," George H. Ruggy and Clayton S. Smith. (Presented by title.)
11. "Chemical Studies on a Physiologically Active Substance in Passiflora Incarnata," George H. Ruggy and C. S. Smith. (Presented by title.)
12. "The Sterol and Resin Alcohols of Gelastrus Scandens," Ole Gisvold. (Presented by title.)
13. "The Constitution of Gelastrol Part II." Ole Gisvold. (Presented by title.)
14. "Crystalline Xanthophyll from Wheat Germ Oil," Ole Gisvold. (Presented by title.)
15. "The Volatile Oil of Poliomintha Incana," A. F. Sievers and C. G. Marshall. (Presented by title.)
16. "A Pharmacognostical Study of Serenoa Serrulata (Saw Palmetto)," B. V. Christensen and R. C. Stokes.
17. "A Crystalline Tannin From the Bark of Acer Spicatum," J. L. Powers and E. L. Cataline.
18. "The Isolation and Identification of Alpha- and Beta-Amyrin from the Bark of Viburnum Opulus," J. L. Powers and W. E. Powers.

SUB-SECTION ON CHEMISTRY.

Wednesday, August 23rd, 3:30 P.M., Room D.

PAPERS.

19. "Method of Assay for Sulfanilamide," R. M. Hitchens and R. W. Towne. (Lantern.)
20. "The Separation and Determination of Aminopyrine in Mixtures," L. E. Warren. (Lantern.)
21. "Studies on Cantharidin I. The Titration of Cantharidin," Benjamin P. Hecht and Lloyd M. Parks.
22. "The Determination of Acetone," Melvin W. Green.
23. "A Study of the Assay of Ginger," Robert Tzucker and C. B. Jordan.
24. "Studies on Cantharides II. The Assay of Cantharides," Benjamin P. Hecht and Lloyd M. Parks.
25. "A Study of the Relative Merits of Permanganate and Cerate Methods in Pharmaceutical Assays," Arthur E. James. (Lantern.)
26. "A Study of the Assay of Strychnine in Tincture of Nux Vomica," Gertrude M. Horn, K. L. Kaufman and S. G. Mittelstaedt. (Lantern.)
27. "Determination of Free Phenols in Methyl Salicylate," R. W. Towne, R. M. Hitchens and M. S. McCauley. (Lantern.)
28. "Fluorescence Analysis as Applied to Some Alkaloids and Crude Drugs," A. Slesser and C. B. Jordan.

29. "A Comparative Study of the Three Recognized Assays for Chenopodium Oil," William F. Reindollar.
30. "An Interferometric Method for the Assay of Nitrous Oxide," Frederick K. Bell and John C. Krantz, Jr.
31. "The Detection of Carbon Monoxide in Medicinal Oxygen," Frederick K. Bell and John C. Krantz, Jr.
32. "A Method for the Determination of Calomel in Tablets," R. A. Bosee and L. A. Perlenfein.
33. "Determination of Nitroglycerin in Concentrated Triturations," George F. Hutchison. (Presented by title.)
34. "Assay of Mild Mercurous Chloride, U. S. P. XI," Ray S. Kelley.
35. "Assay of Potassium Citrate, U. S. P. XI," Ray S. Kelley.
36. "The Heavy Metal Test of the Pharmacopœia," M. W. Carey and R. E. Schoetzow.
37. "Sulfanilamide, Assay of in Tablets," W. E. Honsinger and R. E. Schoetzow.

JOINT SESSION SCIENTIFIC SECTION AND SECTION ON PRACTICAL PHARMACY AND DISPENSING.

Friday, August 25th, 9:30 A.M., Ballroom.

Progress in the Revision of United States Pharmacopœia, E. Fullerton Cook, Chairman. (15 minutes.)

Progress in the Development of National Formulary, E. N. Gathercoal, Chairman. (15 minutes.)

Progress in the Revision of Recipe Book, J. Leon Lascoff, Chairman. (15 minutes).

Report of the Committee on Prescription Tolerances, W. J. Husa, Chairman. (10 minutes.)

Report of the Committee on Weights and Measures, M. N. Ford, Chairman. (10 minutes.)

Second Session—Scientific Section.

Friday, August 25th, 10:30 A.M., Ballroom.

PAPERS.

38. "The Determination of Some Chemical and Physical Constants of Certain Detergents," B. L. Holiday, E. A. Kelly and L. W. Rising.
39. "Preparation of Experimental Salmon Packs for Scientific Investigation," Louis Fischer.
40. "Comparative Study of Vitamins and Constants of Free and Extracted Oil from Canned Sockeye Salmon," Arthur W. Steers and Louis Fischer.
41. "A Study of Athlete's Foot and Its Control," J. B. Vaughan and H. George DeKay.
42. "A Chemical Investigation of Some Florida Volatile Oils," P. A. Foote and A. W. Matthews.
43. "A Study of the Oxidation of Salicylates in Alkaline Solutions," E. A. Brecht and C. H. Rogers.
44. "A Toxic Glycoside of Asclepias Cornuti or the Common Milkweed," A. E. Rihn and H. G. DeKay.
45. "Ointment of Mercuric Nitrate," Rudolph A. Kuever and Carl B. Burnside.
46. "Iodocholeate—Its Efficiency as a Germicide and Its Clinical Performance," Herman R. Scherzer. (Lantern.)
47. "A Study of Ephedrine with Silver Preparations," Donald J. McLeod and H. George DeKay.
48. "Drug Extraction XXII. The Extraction of Podophyllum," William J. Husa and D. W. Lee.
49. "A Study of the Extraction of Astringent Drugs," H. F. Lefevre and C. O. Lee.
50. "The Preparation of Alkaline Bismuth Saccharates," George O. Doak. (Presented by title.)
51. "Colorimetric Determination of Thiamin Chloride in Certain Pharmaceutical Preparations," M. E. Auerbach. (Presented by title.)
52. "Salts of Isopropanolamine I. Triisopropanolamine," George W. Fiero.
53. "Salts of Isopropanolamines II. Mixed Isopropanolamines," George W. Fiero. (Presented by title.)
54. "A Chemical Investigation of the Seeds of Glottidium Vesicarium (Jacq.) Harper," P. A. Foote and L. G. Gramling.
55. "A Comparison of a Rapid Method for the Micro-Determination of Iodine in Thyroid with the U. S. P. XI Method," Charles E. Nicklaus and Nelson Tippett.
56. "A Monograph for Ringer's Solution as a Solvent," Norman Pinschmidt and J. G. Krantz.
57. "Microadaptation of the U. S. P. Method of Analysis to the Official Silver Salts," C. Merrill Brown and Coy W. Waller.
58. "A Study of the Assay of Potassium and Sodium Tartrate," Malcolm J. MacLeod.
59. "The Determination of Iron in Iron Salts of Organic Acids Containing Phosphorus," C. F. Bickford, A. E. Jurist and W. G. Christiansen.
60. "Water in Oil Emulsifying Agents I. (Some Constituents of Lanolin and Similar Compounds)," J. L. Powers, H. B. Leask and R. S. Warner. (Presented by title.)
61. "Chemotherapeutic Studies in the Azobenzene Sulfonchloramide Series. II. Meta and Para Derivatives," Seymour Stern and Abraham Taub. (Lantern.)

Third Session—Scientific Section.

Friday, August 25th, 2:30 P.M., Ballroom.

Report of Committee on Ebert Prize. Glenn L. Jenkins, Chairman.

Report of Committee on Kilmer Prize. H. W. Youngken, Chairman.

Report of Nominating Committee.

PAPERS.

62. "The Assay of Digitalis. I. Criteria for Evaluating the Various Frog Method," Lloyd C. Miller, Herbert A. Braun and Chester I. Bliss. (Lantern.)
63. "A Pharmacologic Study of Devil's Club Root (Fatsia Horrida)," Leonard J. Piccoli, Michael E. Spinapolice and Morris Hecht.
64. "Bioassay of Aconite," B. V. Christensen and John W. Nelson.
65. "The Pharmacology of Soaps II. The Irritant Action on Human Skin," by Byron E. Emery and Leroy D. Edwards. (Lantern.)
66. "The Pharmacology of Soaps III. The Irritant Action of Sodium Alkyl Sulfates on Human Skin," Byron E. Emery and Leroy D. Edwards. (Lantern.)
67. "The Use of Some Medicinal Agents in Reducing Fox Pup Losses at Whelping," F. A. Fuhrman and E. T. Stuhr. (Presented by title.)
68. "The Response of Foxes and Mink to Sex Hormone Administration," F. A. Fuhrman and E. T. Stuhr. (Presented by title.)
69. "Pentobarbital Sodium as an Anesthetic for Mink," F. A. Fuhrman and E. T. Stuhr. (Presented by title.)
70. "The Absorption and Toxicity of Sodium or Potassium Sulfocyanate," Robert C. Anderson and K. K. Chen. (Lantern.)
71. "The Action of Ephedrine on Halogenated Organic Compounds," Frank A. Steldt and K. K. Chen. (Lantern.)
72. "Effect of Introduction of the Halogens into the Phenol Molecule on Toxicity to Goldfish. I. Monochlorophenols," L. E. Smith and W. A. Gersdorff. (Lantern.)
73. "The Local Anesthetic Action of Some Naphthocaines," L. W. Rowe.
74. "Pharmacology of the Thiourethanes," J. M. Dille and P. A. Squires.
75. "Digitalis," Philip Blickensdorfer and H. A. McGuigan.
76. "Synergism between Marihuana and Barbiturates," S. Loewe. (Presented by title.)
77. "A Modification of the Agar Cup Method Suitable for the Estimation of the Fungistatic Action of Powders and Ointments," Arthur E. Meyer. (Presented by title.)
78. "The Pharmacological Action of Tutin," Edward E. Swanson. (Lantern.)
79. "The Pharmacological Relationship of Isomeric Barbituric Acid Derivatives," Edward E. Swanson and W. E. Fry. (Lantern.)
80. "Quantitative Studies on Pain Threshold After Administration of Various Drugs," David I. Macht and Moses B. Macht. (Lantern.)
81. "A Comparative Study of the Method of Action of Quinine Plasmochin and Atabrin in Malarial Treatment," George H. Boyd. (Lantern.)
82. "The U. S. P. XI Digitalis Standard," Orlo F. Swoap and Marvin L. Pabst.
83. "A Study of *p*-Nitrosothymol and *p*-Aminothymol," W. T. Sumerford and Walter H. Hartung. (Lantern.)
84. "Properties, Actions and Possible Medicinal Uses of Elkonite, a Colloidal Clay," M. L. Tainter, G. Kulchar and A. B. Stockton. (Presented by title.)
85. "Non-Interfering Adsorbents in Alkaloidal Analysis," Estelle Koozin Johnson and L. W. Rising.
86. "Volatile Oil of Comptonia Asplenifolium" Romulus DeNicola and E. V. Lynn.
87. "Phenolated Solution of Iodine," Anthony Pulverenti and E. V. Lynn.
88. "Salicyl Mandelic Acid," John Hill and E. V. Lynn.
89. "The Determination of Camphor in Camphor Liniment. An Accurate and Simplified Volatilization Method," Solomon M. Berman.
90. "A Comparative Study of Tannic Acid, U. S. P. XI," Clifton E. Miller and L. W. Rising.
91. "Assays for Iodine and Iodide in Iodine Solutions," Berl S. Alstodt.
92. "Fungus Growths on Alkaloidal Drugs," Fanchon Hart.

Report of Committee on Chairman's Address.
New Business.
Unfinished Business.
Election and Installation of Officers.
Adjournment.

SECTION ON PRACTICAL PHARMACY AND DISPENSING.

(Flash "Ph.")

Chairman, L. W. Richards; *First-Vice-Chairman*, R. W. Clark; *Second Vice-Chairman*, J. K. Attwood; *Secretary*, Louis C. Zopf; *Delegate to the House of Delegates*, W. J. Husa.

First Session, Wednesday, August 23rd, 2:30 P.M., Room F.

Chairman's Address—L. W. Richards.
Secretary's Report—Louis C. Zopf.
Committee Reports.
Appointment of Committees.

PAPERS.

1. "As Ye Sow—So Shall Ye Reap," R. L. Ives.
2. "Back to Pharmacy," Emerson D. Stanley.
3. " ," Charles E. Wilson.
4. "A Prescription Survey," Joe Shine.
5. "The Spring Clean-up," Thelma Morris Coburn.
6. "Trend in Prescribing and What Can Be Done About It," C. L. Guthrie.
7. "Practical Pharmacy," H. E. Henry.
8. "A Suggestion Concerning the Writing of Prescriptions," Joseph P. Miale.
9. "On Building Prescription Business," J. W. Snowden.
10. "Qualifications of the Personnel for a Professional Pharmacy," J. K. Attwood.
11. "Milwaukee Prescription Pricing Survey," Emil C. Horn.

JOINT SESSION WITH SCIENTIFIC SECTION.

Friday, August 25th, 9:30 A.M., Ballroom.

(See program of Scientific Section.)

Second Session, Friday, August 25th, 2:30 P.M., Room F.

PAPERS.

12. "A Rapid Procedure for the Manufacture of Saponated Solution of Cresol," Lawell F. Martin and William A. Prout.
13. "The Status of Phenol in Ointment of Phenol U. S. P.," William A. Prout and A. Clifton Smith, Jr.
14. "Sulfanated Oils," Paul Soderdahl.
15. "Incompatibilities in Prescription III—The Use of Inert Powders in Capsules to Prevent Liquefaction Due to Formation of a Eutectic Mixture," William J. Husa and Charles H. Becker.
16. "Incompatibilities in Prescriptions IV—The Use of Inert Powders in Capsules to Prevent Liquefaction Due to Deliquescence," William J. Husa and Charles H. Becker.
17. "Pastes for Dermatologic Use," Bernard Fantus, M.D., and H. A. Dyniewicz.
18. "A Study of Hydrophile Ointment Bases and Their Application in Preparing Official Ointments," G. W. Johnston and C. O. Lee.
19. "Hydrogenated Oil as an Ointment Base II," George W. Fiero.
20. "Hydrogenated Oil as an Ointment Base III—Potassium Iodide Ointment," George W. Fiero.
21. "Hydrogenated Castor Oil as an Ointment Base IV—Hydroxystearic Acid," George W. Fiero.
22. " ," Earl P. Guth.
23. "Publisher's Side of Pharmaceutical Literature," William E. Kirsch.
24. "Paradoxical Posology," Wilbur L. Scoville.
25. "Syrup of Wild Cherry in Prescriptions," C. C. Reed, P. L. Burrin and F. E. Bibbins.
26. "Preliminary Report of the Manufacture of Magma Magnesiæ by Hydrolysis," F. Stein, G. Bornstein and L. D. Fonda.
27. "An Unusual Feature of the University of Washington Method for Teaching Dispensing Pharmacy," E. M. Plein and L. W. Rising.
28. "What Is Professional Pharmacy? Tentative Definitions and Plan to Establish Its Status," L. F. Kebler.

New Business.

Election of Officers.

Reports of Committees.

Adjournment.

SUB-SECTION ON HOSPITAL PHARMACY.

(Flash "Hosp.")

Chairman, I. T. Reamer; *First Vice-Chairman*, Hazel E. Landeen; *Secretary*, S. W. Morrison.

First Session, Thursday, August 24th, 2:30 P.M., Room C.

Call to Order.
Appointment of Committees.

1. Chairman's Address.

PAPERS.

2. "Pricing Hospital Medication," Hazel E. Landeen.
3. "Endocrines, a Practical Knowledge for the Hospital Pharmacist," A. R. Bliss.
4. "Pharmacy in a Children's Hospital," Margaret Pearson.
5. "Our Hospital Pharmacists Association," R. H. Stimson.
6. "Stock Control," F. F. Hansman.

Second Session, Friday, August 25th, 10:30 A.M., Room C.

PAPERS.

7. "Effect of Changes in the Formula of Liq. Antisepticus N. F. VI," L. W. Busse.
8. "The Hospital Pharmacist and the Intern," Lowell Ruff.
9. "Divided We Fall," Miss B. Lehrke.
10. "Some Values in the Use of Formularies," H. C. Hillhouse.
11. "A Hospital Formulary and Its Effect on Costs," Mabel M. Newquist.
12. "Manufacturing Intravenous Solutions," J. F. Lyon.
13. "Ampul Manufacture," D. A. Clarke.
14. "The Hospital Pharmacy and the Diabetic," Mitchell Stocklosa.
15. "Narcotic Control," Mary E. Bowen.

SECTION ON EDUCATION AND LEGISLATION.

(Flash "E.")

Chairman, J. F. McCloskey; *Vice-Chairman*, A. O. Mickelsen; *Secretary*, L. M. Ohmart; *Delegate to the House of Delegates*, George A. Moulton.

First Session, Wednesday, August 23rd, 2:30 P.M., Pompeian Room.

Chairman's Address—J. F. McCloskey.
Secretary's Report—L. M. Ohmart.
Appointment of Committees.

SYMPOSIUM ON NATIONAL AND STATE LEGISLATION.

1. E. F. Kelly, *Secretary*, AMERICAN PHARMACEUTICAL ASSOCIATION.
2. G. A. Moulton, *President*, New Hampshire State Pharm. Association.
3. O. F. Cook, *Secretary*, Michigan State Pharm. Association.

4. P. R. Loveland, *Secretary*, New Jersey State Pharm. Association.
5. J. J. Shine, *Secretary*, Illinois State Pharm. Association.
6. T. C. Sharp, *Secretary*, Tennessee State Pharm. Association.
7. J. G. Beard, *Secretary*, North Carolina State Pharm. Association.
8. W. J. Danforth, *Secretary*, Texas State Pharm. Association.
9. C. E. Rickard, *Secretary*, Pennsylvania State Pharm. Association.
10. N. M. Ford, *Secretary*, Ohio State Pharmaceutical Association.
11. Mrs. C. B. Miller, *Secretary*, Kansas State Pharm. Association.
12. L. M. Kantner, *President*, Maryland Board of Pharmacy.
13. J. L. Weinland, *Secretary*, Indiana State Pharm. Association.
14. C. B. Goldthwaite, *Secretary*, Alabama State Pharm. Association.
15. G. W. Mather, *Secretary*, New York State Pharm. Association.

Second Session, Friday, August 25th, 9:30 A.M., Pompeian Room.

PAPERS.

1. "Pharmaceutical Jurisprudence in the College of Pharmacy Curriculum," Robert L. Swain.
2. "A Pharmacy Course and a Pharmacy Degree to Meet Our Present Needs," Robert P. Fischelis.
3. "Why a Pharmaceutical Education?" Howard C. Newton.
4. "Incompatibilities in Prescriptions, II," William J. Husa.
5. "An Educational Philosophy—We Have None," Frederick J. Wulling.
6. "The Pharmacy Student and Employment, II," C. W. Ballard.

Unfinished Business.
Report of Committees.
Election and Installation of Officers.
Adjournment.

SECTION ON PHARMACEUTICAL ECONOMICS.

(Flash "Co.")

Chairman, Paul C. Olsen; *Secretary*, Joseph H. Goodness; *Vice-Chairman*, B. Olive Cole; and *Delegate to the House of Delegates*, Henry F. Hein.

First Session, Wednesday, August 23rd, 2:30 P.M., Room G.

Chairman's Address—Paul C. Olsen.
Report of the Secretary.
Appointment of Committees.

PAPERS.

1. "Are We Afraid?" Clarence M. Brown.
2. "New Labels *vs.* Old Labels," Samuel Shkolnik.
3. "Pharmacy's Economic Service," John N. McDonnell.
4. "What Is a Prescription?" Joseph H. Goodness.
5. "Working Hours of a Pharmacist," John F. McCloskey.

Second Session, Friday, August 25th, 2:30 P.M., Room G.

PAPERS.

6. "Insecticides in the Drug Store," Maynard W. Quimby.
7. "Hiring Unregistered Drug Clerks," Clarence M. Brown.
8. "1939 Prescription Survey," Joseph H. Goodness.

Symposium: Federal and State Food, Drug and Cosmetic Laws and the Retail Pharmacist.
Reports of Committees.
Election and Installation of Officers.
Adjournment.

SECTION ON HISTORICAL PHARMACY.

(Flash "Hi.")

Chairman, Willis T. Bradley; *Secretary*, J. Hampton Hoch; *Delegate to the House of Delegates*, E. J. Ireland; *Historian*, E. G. Eberle.

A brief Memorial Meeting will be held during the Second General Session of the A. PH. A. on Thursday forenoon.

First Session, Wednesday, August 23rd, 2:30 P.M., Room A.

Chairman's Address—W. T. Bradley.
Secretary's Report—J. Hampton Hoch.
Report of Historian—E. G. Eberle.
Report of the Delegate to the House of Delegates, E. J. Ireland.

PAPERS.

Committee Reports.

1. "Psychic Medicine," Charles Whitebread.
2. "History of Pharmacy in the U. S. from 1492 to 1821," H. Colle.
3. "Baltimoreans and the First National Pharmacopœia," C. K. Deischer.
4. "The Wetherill Family in Philadelphia Pharmacy," J. E. Kramer.
5. "The Squibb Ancient Pharmacy," G. Urdang and F. W. Nitardy.
6. "Books Make History in Pharmacy," G. Urdang and F. W. Nitardy.
7. "Pharmacy as a Subject of Religious Influence and Feeling," G. Urdang and F. W. Nitardy.
8. "Establishing the Drug Laboratory in the Bureau of Chemistry, United States Department of Agriculture," L. F. Kebler.

Second Session, Friday, August 25th, 2:30 P.M., Room A.

Miscellaneous Business.

PAPERS.

1. "Personal Reminiscences of Prof. John J. Abel," D. I. Macht.
2. "The Congress of the International Federation of Pharmacy. Observations and Impressions," Rudolf Wallner.

3. "An Account of the Attempt of the Society of Apothecaries to Establish the Drug Trade in Colonial Georgia," J. Krafka, Jr.
4. "Early Relation of Pharmacy and Medicine in the U. S.," F. E. Kredel and J. H. Hoch.
5. "Historical Items of Pharmacy in Montana," C. E. Mollett.
6. "History of Pharmacy in Oregon," A. Ziefle.
7. "M. E. Chevreul, The Fiftieth Anniversary of His Death," M. E. Weeks and L. O. Amberg.

Address, "Lister's Contribution to the Development of Antisepsis," Hillyer Rudisill, Jr.

Election of Officers.
Final Business.

CONFERENCE OF PHARMACEUTICAL ASSOCIATION SECRETARIES.

THIRTEEENTH ANNUAL MEETING.

President, Irl Brite; *First Vice-President*, J. B. Slocum; *Second Vice-President*, Mrs. C. B. Miller; *Secretary-Treasurer*, J. Lester Hayman; *Delegate to the House of Delegates*, Jos. J. Shine; *Members of the Executive Committee:* J. Lester Hayman, Otis F. Cook, P. R. Loveland.

First Session, Wednesday, August 23rd, 2:30 P.M., Room B.

Call to Order.
Calling the Roll.
Reading the Minutes.
President's Address—P. R. Loveland.
Appointment of Committees.
Report of Officers.
Reading of Communications.
Report of Committee on Membership.
Subjects for Discussions.

1. What is the situation in regard to co-ops. in your state?
2. What is your situation in regard to fair trade?
3. How will the State or Federal Food, Drug & Cosmetic Acts affect your members?
4. Is your financial income sufficient to carry out your association programs? Should your program be extended? How?
5. Can State Associations do anything concerning the elimination of the 10% wholesaler discounts?
6. What can or are you doing concerning the distribution of drug products through non-drug outlets?
7. Health Legislation. Are your pharmacists receiving their fair share of relief funds being spent for medicinals? For medicinals freely distributed to those with venereal diseases?
8. What part will your office play in the Federal investigation of Fair Trade Acts?
9. Do you have any problems concerning the publication of state journals?
10. What has been your experience in regard to Professional Relation Programs? Are they successful? Should they be extended?
11. Food and Drug Legislation.
12. U. S. P.-N. F. Promotion.
13. Public Relations.
14. Pharmacy Week and First Aid Week.
15. Improvements in the Form of Organization of State Associations—Simplification of Committees.
16. What is the most effective method of obtaining New Members? Of holding Old Members?
17. What are the State Associations doing in regard to Compulsory Health Insurance?

Second Session, Friday, August 25th, 2:30 P.M., Room B.

Continuation of Discussions.
Election of Members.
Election of Officers.
Miscellaneous Business.
Unfinished Business.
Installation of Officers.
Adjournment.

CONFERENCE OF PHARMACEUTICAL LAW ENFORCEMENT OFFICIALS.

ELEVENTH ANNUAL MEETING.

Chairman, R. L. Swain; *Secretary*, M. N. Ford; *Delegate to the House of Delegates*, F. C. Schaefer.

First Session, Monday, August 21st, 8:30 P.M., Room F.

1. Call to Order.
2. Remarks by Chairman, Robert L. Swain.
3. Report of Secretary, M. N. Ford.
4. Report of Finance Committee, Frederick C. A. Schaefer.
5. Appointment of Conference Committees.
6. Symposium on the Federal Food, Drug and Cosmetic Act.
   (*a*) "Extension of Federal Control Over Drugs and Cosmetics," R. L. Swain.
   (*b*) "Adulteration," R. P. Fischelis.
   (*c*) "Misbranding, Including Dangerous Drugs," Hugo Schaefer.
   (*d*) "New Drugs," Joseph H. Goodness.
   (*e*) "The Wheeler Lea Act As It Applies to Drugs and Cosmetics," Samuel Shkolnik.
7. Symposium on State Food, Drug and Cosmetics Acts.
   (*a*) Discussion by states which have adopted acts similar to the Federal Act.
   (*b*) Discussion by states which have not adopted acts similar to the Federal Act.

Second Session, Thursday, August 24th, 2:30 P.M. Room F.

1. Symposium on Law Enforcement in Georgia and the Nearby States, Alabama, Florida, Kentucky, Louisiana, North Carolina, South Carolina and Tennessee. Discussion led by S. H. Dretzka.
2. Round Table Discussion of a More Effective Control Over the Distribution of Drugs and Medicines. Discussion will be opened by Robert P. Fischelis.

Unfinished Business.
Election and Installation of Officers.
Adjournment.

CONFERENCE OF STATE COMMITTEES ON U. S. P.-N. F. PROMOTION.

Chairman, Marvin J. Andrews; *Secretary*, Charles V. Selby.

Thursday, August 24th, 2:30 P.M., Room A.

1. "The New Series of Articles to Be Prepared by the U. S. P. Revision Committee in Coöperation with the American Medical Association," E. F. Cook.
2. "Activities of the N. A. R. D. Committee on Interprofessional Relations," O. U. Sisson.
3. "U. S. P.-N. F. Publicity in West Virginia," Charles V. Selby.
4. "U. S. P.-N. F. Publicity in South Carolina," W. D. Strother.
5. "Professional Relations in Wisconsin," Max N. Lemberger.
6. "Personal Contact Methods as Used in New Mexico," H. E. Henry.
7. "New Jersey Formulary," W. R. Rickart.

CONFERENCE OF PROFESSIONAL PHARMACISTS.

Thursday, August 24th, 2:30 P.M., Room G.

1. Introductory Remarks: C. B. Jordan, Purdue University; J. Leon Lascoff, President, A. Ph. A.; E. F. Kelly, Secretary, A. Ph. A.
2. "A Need for an Association of Exclusive Prescription Pharmacists," A. L. Malmo.
3. "Pharmacist, Physician and Patient," Erich E. Kunze.
4. "An Appeal for Professional Pharmacies," A. A. Hoehn.
5. "A Bundle of Sticks," Leroy A. Weidle.
6. "Professional Pharmacists' Contact with Physicians," T. C. Marshall.
7. "Medicine by Remote Control," Joseph T. Matousek.
8. "Advertising the Ethical Pharmacy," Walding G. Rupp.
9. "Professional Pharmacy, Its Relation to Modern Medicine," J. E. Griffin.
10. "The Pharmacy of Vitamin B_1," L. Greengard.
11. "Possibilities of a Professional Pharmacists' Organization within the A. Ph. A.," Mark W. Judge.
12. "The Professional Druggist *vs.* To-day's Drug Business," William Kersten.

THE PLANT SCIENCE SEMINAR.

SEVENTEENTH ANNUAL MEETING.

August 14th to 19th.

Chairman, Earl F. Fischer; *Secretary-Treasurer*, Elmer H. Wirth; *Local Secretary*, J. Hampton Hoch; *Council Members*, F. J. Bacon and L. K. Darbaker.

Monday, August 14th.

Registration at Blue Ridge College, Blue Ridge, N. C.

2:00 P.M. Botanizing trip through Blue Ridge College grounds, led by Dr. Kessler.

8:00 P.M. Address by Mr. W. W. Bell and motion pictures of various phases of activity in the crude drug field.

Tuesday, August 15th.

9:00 A.M. Call to order by Vice-Chairman, Prof. E. B. Fischer.
Address of Welcome, Dr. W. D. Weatherford, President of Blue Ridge College.
Announcements and Appointments.
Program of Papers.

11:30 A.M. Luncheon.

1:00 P.M. Visit to S. B. Penick & Co.'s Asheville warehouse. Demonstrations of various operations.

8:00 P.M. Address by Miss Carroll, "The Relationship of Art to Botany."

Wednesday, August 16th.

8:30 A.M. Trip to Mt. Mitchell *via* toll road. Box lunch at summit. Return *via* Biological Survey Reservation. Botanizing led by Mr. F. J. le Clair and Dr. Totten.

8:30 P.M. Motion pictures of previous Seminars, L. K. Darbaker and Prof. E. H. Wirth.

Thursday, August 17th.

9:00 A.M. Program of papers and Round Table discussion.

11:00 A.M. Trip through Biltmore Forest. Lunch at Biltmore Dairy. Tour through Manor House and Museum on Biltmore Estate.

8:00 P.M. Final business meeting.
Committee reports and election of officers.

8:30 P.M. Address by Dr. Totten, "The Trees of North Carolina Mountains."

Friday and Saturday, August 18th and 19th.

Available for visits to Chapel Hill, N. C., or to Charleston, S. C.

Sunday, August 20th.

Leave Chapel Hill, Charleston or Blue Ridge for Atlanta.

THE NATIONAL CONFERENCE ON PHARMACEUTICAL RESEARCH.

SEVENTEENTH ANNUAL MEETING.

Chairman, Wm. J. Husa; *Vice-Chairman*, H. W. Youngken; *Secretary*, John C. Krantz, Jr.; *Treasurer*, Fitzgerald Dunning; *Executive Committee*, H. V. Arny, James C. Munch, Francis E. Bibbins.

First Session, Tuesday, August 22nd, 2:00 P.M., Room G.

2:00 P.M. Call to Order by the Chairman.
2:01 P.M. Appointment of Nominating Committee.
2:03 P.M. Reports of Officers.

SYMPOSIUM ON TRAINING OF RESEARCH MEN IN PHARMACY.

2:15 P.M. "Training of Research Men in Universities," Glenn L. Jenkins.
2:30 P.M. "The Florida Plan of Research Training," W. J. Husa.
2:45 P.M. "Types of Research Training Desired by Research Institutions," George D. Beal.
3:00 P.M. "Types of Research Training Desired by Pharmaceutical Manufacturers," F. O. Taylor.
3:15 P.M. General discussion of "Training of Research Men in Pharmacy."
3:45 P.M. Address, "Recent Advances in Chemical Therapy," Randolph Major.
4:30 P.M. Discussion of Address.
4:45 P.M. Roll Call of Delegates.
4:50 P.M. Election and Installation of Officers.
5:00 P.M. Adjournment.
6:00 P.M. Annual Dinner.
7:00 P.M. Address, "Recent Investigations on the Toxicity of Nicotine," H. B. Haag.
8:00 P.M. Adjournment.

THE AMERICAN ASSOCIATION OF COLLEGES OF PHARMACY.

FORTIETH ANNUAL MEETING.

President, Earl R. Serles; *Vice-President*, James M. Dille; *Secretary-Treasurer*, Zada M. Cooper; *Chairman of the Executive Committee*, Ernest Little.

Monday, August 21st.

9:00 A.M. Meeting of the Executive Committee. Room A.
9:30 A.M. Teachers Conferences.
1:30 P.M. First Session—Business. Pompeian Room.
6:30 P.M. Annual Dinner. Ballroom.
8:00 P.M. Second Session—Panel Discussion. Pompeian Room.

CONFERENCE OF TEACHERS OF PHARMACY.

Chairman, Elmer L. Hammond; *Vice-Chairman*, D. B. R. Johnson; *Secretary*, Wm. A. Jarrett.

Monday, August 21st, 9:30 A.M., Room C.

Discussion Topic: The Educational Function of Teachers of Pharmacy

1. "A History of the Teachers of Pharmacy."
2. "The Function of Teachers of Pharmacy toward the Retail and Manufacturing Fields," Marvin J. Andrews.
3. "The Function of Teachers of Pharmacy toward Research Work," L. Wait Rising.
4. "The Function of Teachers of Pharmacy toward the Teaching Profession," R. C. Wilson.
5. "Modern Educational Methods and Trends," Paul R. Morrow.

CONFERENCE OF TEACHERS OF CHEMISTRY.

Chairman, G. A. Bergy; *Vice-Chairman*, H. G. DeKay; *Secretary*, F. Scott Burkey.

Monday, August 21st, 9:30 A.M., Room F.

1. "How Much Organic Chemistry Does the Present Day Pharmacy Student Need?" G. W. Hargreaves.
2. "Pharmaceutical Chemistry in a Flexible Curriculum," George L. Webster.
3. "Chemistry Courses in Colleges of Pharmacy," Walter H. Hartung.
4. "The Teaching of Qualitative and Quantitative Analysis in Pharmacy Schools," H. George DeKay.

CONFERENCE OF TEACHERS OF PHARMACOGNOSY AND PHARMACOLOGY.

Chairman, M. S. Dunn; *Secretary*, J. Hampton Hoch.

Monday, August 21st, 9:30 A.M., Room B.

Discussion Topic: The Aims and Objectives of the Course in Pharmacology and Pharmacognosy and How to Attain Them."

1. "Pharmacology," A. Richard Bliss, L. David Hiner, James M. Dille, W. H. Zeigler.
2. "Pharmacognosy," Edmund N. Gathercoal, Franklin J. Bacon, A. John Schwarz, R. S. Justice.

CONFERENCE OF TEACHERS OF PHARMACEUTICAL ECONOMICS.

Chairman, F. D. Lascoff; *Secretary*, B. Olive Cole.

Monday, August 21st, 9:30 A.M., Room G.

1. "Accounting Theory and Practice for Pharmacy Students," Paul C. Olsen.
2. "Six Years in a Practice Pharmacy," M. Medford Cooper.

3. "Developing the Prescription Business in a Pharmacy," Ralph W. Clark.
4. "What Economics Offers to the Pharmacy Curriculum," John V. Connor.
5. "Term Papers for Commercial Pharmacy," Clarence M. Brown.
6. "Education and Creation in Pharmacy Business Courses," J. H. Goodness.
7. "Pharmaceutical Economics?" Karl Scholz.
8. "Main Street (visiomatic)," Coca-Cola Company.
9. "Textbook for Pharmaceutical Economics," E. L. Newcomb.

SESSIONS OF THE ASSOCIATION.

First Session, Monday, August 21st, 1:30 P.M., Pompeian Room.

Roll Call.
Appointment of Committee on Resolutions.
Address of the President—Earl R. Serles.
Report of the Secretary-Treasurer, Zada M. Cooper.
Report of the Executive Committee, Ernest Little.
Appointment of Nominating Committee.
Appointment of Auditing Committee.
Reports of Standing Committees:
Committee on Educational and Membership Standards, A. G. DuMez.
Committee on Curriculum and Teaching Methods, Henry M. Burlage.
Committee on Activities of Students and Alumni, R. E. Terry.
Delegates to the American Council on Education, Rufus A. Lyman.
Committee on Relation of Boards and Colleges, H. Evert Kendig.
Committee on Libraries, Charles O. Lee.
Committee on Problems and Plans, Rufus A. Lyman.

Monday, August 21st, 6:30 P.M., Ballroom.

Joint Annual Dinner with N. A. B. P.
Address by Chancellor S. V. Sanford, University System of Georgia, "Pharmacy of Tomorrow."

Second Session, Monday, August 21st, 8:00 P.M., Pompeian Room.

Panel Discussion—Leader, Hugh C. Muldoon. Professional Relations.

1. Relationship with Physicians, Marvin J. Andrews.
2. Relationship with Dentists, George C. Schicks.
3. Relationship with Hospitals and Nurses, Louis C. Zopf.
4. Relationship with The Public and Other Pharmacists, Clark T. Eidsmoe.

Tuesday, August 22nd, 9:30 A.M., Ballroom.

Joint Session of the AMERICAN PHARMACEUTICAL ASSOCIATION, the National Association of Boards of Pharmacy and the American Association of Colleges of Pharmacy. (See program National Association Boards of Pharmacy.)

Third Session, Tuesday, August 22nd, 2:00 P.M., Pompeian Room.

1. Recommendations from the Teachers' Conferences.
2. Report of the Editor of the *American Journal of Pharmaceutical Education*, Rufus A. Lyman.
3. Reports of Special Committees:
   (1) Committee on Predictive and Achievement Tests, Carl J. Klemme.
   (2) Committee on Professional Relations, George C. Schicks.
4. Reports of Special Representatives:
   (1) Progress of Medicinal Plant Survey, H. W. Youngken.
   (2) Biological Abstracts, Heber W. Youngken.
   (3) Representatives to the National Drug Trade Conference, W. F. Rudd.
   (4) Abstract of paper, "Commercial Problems of the Pharmacist—a Textbook," E. L. Newcomb.
   (5) Representatives to National Conference on Pharmaceutical Research, A. John Schwarz.
   (6) Representatives to the Druggists Research Bureau, Paul C. Olsen.
   (7) Representative to the National Association of Retail Druggists, Geo. L. Webster.
   (8) Representative to the National Wholesale Druggists Association, Ivor Griffith.
5. Report of the Historian.
6. Report of the Committee on Resolutions.
7. Report of the Auditing Committee.
8. Unfinished Business.
9. Miscellaneous Business.
10. Election of Officers.
11. New Business.
12. Executive Session.

NATIONAL ASSOCIATION OF BOARDS OF PHARMACY.

THIRTY-SIXTH ANNUAL CONVENTION.

President, Roy Bird Cook; *Honorary President*, E. V. Zoeller; *Treasurer*, J. W. Gayle; *Secretary*, H. C. Christensen.

First Session, Monday, August 21st, 9:30 A.M., Ballroom.

1. Call to Order, President Roy Bird Cook.
2. Welcome, C. D. Jordan.
3. Roll Call, Secretary H. C. Christensen.
4. Appointment of Committee on Credentials, President Roy Bird Cook.
5. President's Address, Roy Bird Cook.
6. Report of Secretary, H. C. Christensen.
7. Report of Treasurer, J. W. Gayle.
8. Appointment of Nominating Committee, President Cook.
9. Report of Executive Committee, Chairman W. Mac Childs.

10. N. A. B. P. Banquet Announcement.
11. Officers' Luncheon for new members only, 12:30 P.M.

Second Session, Monday, August 21st, 1:30 P.M., Ballroom.

1. Report of Legislative Committee, Chairman Charles B. Rohrer.
2. Report of Committee on National Legislation, Chairman A. L. I. Winne.
3. Report of Committee on Prerequisite Legislation, Chairman Geo. A. Moulton.
4. Report of Publicity Committee, Chairman Kenneth Jones.
5. Report of Grievance Committee, Chairman P. H. Brady.
6. Report of Committee on Minimum Standards on Technical Equipment, Chairman A. C. Taylor.
7. Report of Committee on Study and Correlation of Practical Experience Requirements, R. P. Fischelis.
8. Report of Special Committee on Practical Examination, A. L. I. Winne.

N. A. B. P. AND A. A. C. P. DINNER.

Monday, August 21st, 6:30 P.M., Ballroom.

Speaker: Chancellor S. V. Sanford, University System of Georgia, "Pharmacy of Tomorrow."

JOINT SESSION WITH AMERICAN ASSOCIATION OF COLLEGES OF PHARMACY AND AMERICAN PHARMACEUTICAL ASSOCIATION.

Tuesday, August 22nd, 9:30 A.M., Ballroom.

1. Report of the Fairchild Scholarship Committee, E. G. Eberle.
2. Report of the Committee on Pharmaceutical Syllabus, Henry M. Burlage.
3. Report of the American Council on Pharmaceutical Education, A. G. DuMez.
4. Report of the Committee on Status of Pharmacists in the Government Service, H. Evert Kendig.
5. Report of the Committee on Modernization of Pharmacy Laws, Robert L. Swain.
6. "The Pharmacist as an Educational Influence in Community Life," Walter D. Cocking.
7. Discussion, "The Necessity of Maintaining Adequate Professional Standards in Pharmacy," George A. Moulton, J. G. Beard and Walter H. Cousins.

Final Session, Tuesday, August 22nd, 2:00 P.M., Ballroom.

1. Reports of Vice-President:
   District No. 1....A. Norman La Salle
   District No. 2....C. L. Guthrie
   District No. 3....Paul Molyneux
   District No. 4....S. H. Dretzka
   District No. 5....R. L. Whaley
   District No. 6....W. A. Worner
   District No. 7....W. A. Woehner*
   District No. 8....Linn E. Jones
2. Report of Committee on Constitution and By-Laws, L. C. Lewis.
3. Report of Resolutions Committee, A. C. Taylor.
4. Reports of Special Committees.
5. Unfinished Business.
6. New Business.
7. Report of Nominating Committee.
8. Election and Installation of Officers.
9. Adjournment.

GENERAL ENTERTAINMENT PROGRAM.

(Please wear your Convention Badge and have tickets with you.)

SUNDAY, August 20th, 8:00 P.M.—Opening Concert, Negro Choir in Garden of Hotel.

WEDNESDAY, August 23rd, 7:30 P.M.—Joint Banquet, Piedmont Driving Club.

THURSDAY, August 24th, 6:00 P.M.—Barbecue on the Grounds of the Atlanta Biltmore Hotel.

FRIDAY, August 25th, 10:30 P.M.—Cotton Ball. Ballroom. Cotton Souvenirs.

PROGRAM FOR THE ENTERTAINMENT OF THE LADIES.

MONDAY, August 21st, 1 P.M.—Luncheon.

TUESDAY, August 22nd, 5:00 to 7:00 P.M.—Tea at Governor's Mansion.

THURSDAY, August 24th, 10:00 A.M.—Tour of the residential section of Atlanta including stop at Cyclorama.
1:00 P.M.—Luncheon. Place to be decided.

FRIDAY, August 25th, 9:00 A.M.—Trip to Griffin, 40 miles, in private cars, to visit cotton mills. Picnic luncheon at Griffin.

CHAIRMEN OF COMMITTEES.

General Chairman and Local Secretary—R. C. Wilson.

Know Georgia—R. C. Coleman. House—D. W. Leary. Finance—T. C. Marshall. Banquet and Barbecue—L. N. Camp. Publicity—R. D. Rainey. Registration—L. R. Brewer. Reception—A. H. Waldon. Entertainment—C. H. Evans.

LADIES' COMMITTEE.

Atlanta General Chairlady—Mrs. W. J. Gower.
Vice-Chairlady—Mrs. D. W. Leary.

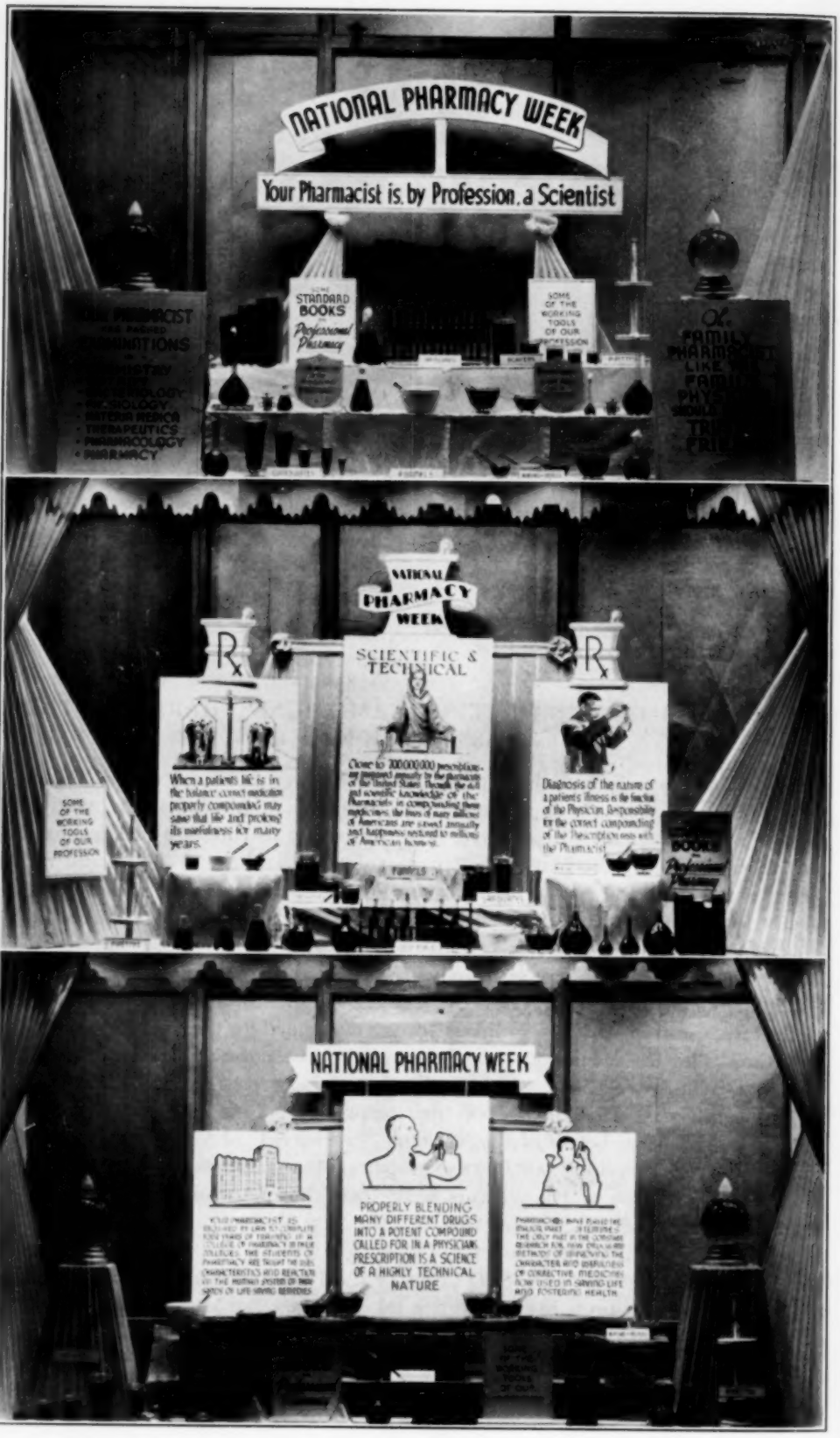
* Deceased.

CUBAN PHARMACISTS VISIT THE AMERICAN PHARMACEUTICAL ASSOCIATION.

On Thursday, July 27th, a party of Cuban pharmacists and their friends, shown in the picture above, inspected the American Institute of Pharmacy and the activities being carried on there. The visit was a feature of a professional excursion organized by the National Pharmaceutical Association of Cuba and which included a trip to the New York World's Fair. The Cuban Association was officially represented by its President, Dr. Raul Romero Jordan, and its Secretary General, Dr. Jorge A. Dominicis, both of Havana.

In the absence of Secretary Kelly, the visitors were received by Chairman Hilton of the Council of the A. PH. A. who extended them a cordial welcome, and by the Headquarters' staff. President Jordan responded for the visitors, expressing their thanks for the many courtesies being paid them and the earnest desire that the very friendly relations which have existed between the two organizations will continue. As an evidence of their appreciation and cordial good wishes President Jordan, on behalf of the National Pharmaceutical Association, presented a Cuban flag to the AMERICAN PHARMACEUTICAL ASSOCIATION which was accepted by Chairman Hilton. The visitors were then shown through the building by members of the staff, after which they left for New York.

Dr. Hugh S. Cumming, Director, Dr. A. A. Moll, Secretary, Mr. L. Marquez, Mr. R. H. Martinez and Mrs. S. O'Leary of the Pan American Sanitary Bureau, were also present to assist in entertaining the visitors. Dr. Moll very kindly acted as interpreter when this was required.


NATIONAL PHARMACY WEEK
Your Pharmacist is by Profession, a Scientist
STANDARD BOOKS
Professional Pharmacy
SOME OF THE WORKING TOOLS OF OUR PROFESSION
· PHARMACY
NATIONAL PHARMACY WEEK
SCIENTIFIC & TECHNICAL
Rx
Rx
When a patient's life is in the balance correct medication properly compounded may save that life and prolong its usefulness for many years.
Close to 300,000,000 prescriptions are compounded annually by the pharmacists of the United States. Through the skill and scientific knowledge of the Pharmacists in compounding these prescriptions the lives of many millions of Americans are saved annually and happiness restored to millions of American homes.
Diagnosis of the cause of a patient's illness is the function of the Physician. Responsibility for the correct compounding of the Prescription rests with the Pharmacist.
SOME OF THE WORKING TOOLS OF OUR PROFESSION
BOOKS
NATIONAL PHARMACY WEEK
PROPERLY BLENDING MANY DIFFERENT DRUGS INTO A POTENT COMPOUND CALLED FOR IN A PHYSICIAN'S PRESCRIPTION IS A SCIENCE OF A HIGHLY TECHNICAL NATURE